New Dammarane-Type Saponins from the Rhizomes of *Panax japonicus*

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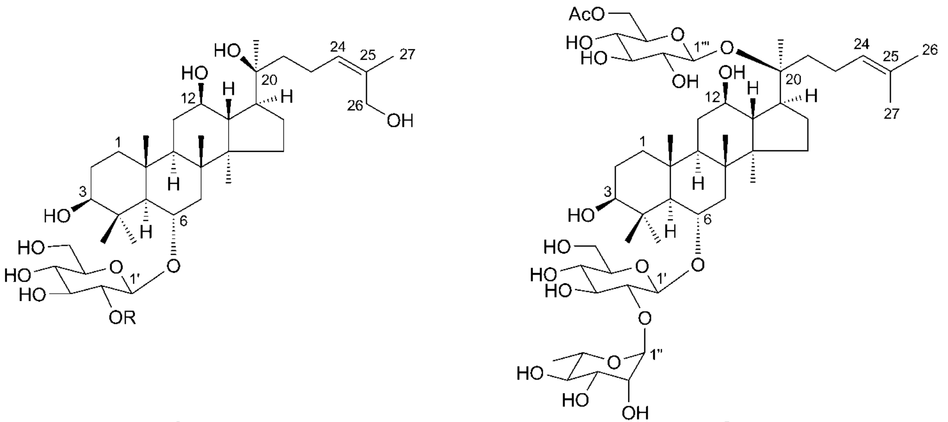
Phytochemical investigation of the rhizomes of *Panax japonicus* C. A. MEYER (Araliaceae) resulted in the isolation of two new dammarane-type triterpenoid saponins, yesanchinoside R_1 (**1**) and yesanchinoside R_2 (**2**), together with one new natural product, 6‴-*O*-acetylginsenoside Re (**3**). In addition, 25 known compounds, including 23 triterpenoid saponins, **4**–**26**, *β*-sitosterol 3-*O*-*β*-D-glucopyranoside (**27**), and ecdysterone (**28**), were also identified. The known saponins **12**, **15**, and **18**–**22** were reported for the first time from the title plant. Their structures were elucidated on the basis of detailed spectroscopic analyses, including 1D- and 2D-NMR techniques, as well as acidic hydrolysis.

Introduction. – *Panax japonicus* C. A. MEYER (Araliaceae), Chinese name '*Zhu-Jie-Shen*', belongs to the same genus of ginseng (*P. ginseng* C. A. MEYER), American ginseng (*P. quinquefolius* L.), and notoginseng (*P. notoginseng* (BURK.) F. H. CHEN), all of which are famous medicinal herbs. The rhizome, recorded in the Chinese Pharmacopoeia, is used for enhancing immunity, diminishing inflammation, and transforming phlegm [1]. It is also used medicinally in Japan, Korea, and Europe for the treatment of lifestyle-related diseases, such as high-fat-diet-induced obesity [2] and alcohol-induced gastric ulcer [3]. Oleanane- and dammarane-type triterpenoid saponins were reported to be the characteristic components of this herb [4][5]. It was found that the dammarane-type saponin compositions of the rhizomes of *P. japonicus* collected from different regions were remarkably different from each other [5]. As part of our continuing research on chemical constituents of medicinal plants from the genus *Panax*, a detailed phytochemical investigation of the rhizomes of *P. japonicus*, collected in Gao-Li-Gong Mountain in Yunnan, China, was carried out. This led to the isolation of two new minor dammarane-type triterpenoid saponins, yesanchinosides R_1 and R_2 (**1** and **2**, resp.), and a new natural product, 6‴-*O*-acetylginsenoside Re (**3**; *Fig. 1*), in addition to 25 known compounds. Here, we describe the isolation and structure elucidation of the new compounds based on detailed spectroscopic analyses and acidic hydrolysis.

Results and Discussion. – The MeOH extract of the fresh rhizomes of *P. japonicus* was subjected to various column chromatographies, including *Diaion HP20SS*, *MCI-gel CHP20P*, *RP-18*, and silica gel, to afford 28 compounds, **1**–**28** (*Figs. 1* and *2*). Of them,



1 R = H
2 R = Xyl

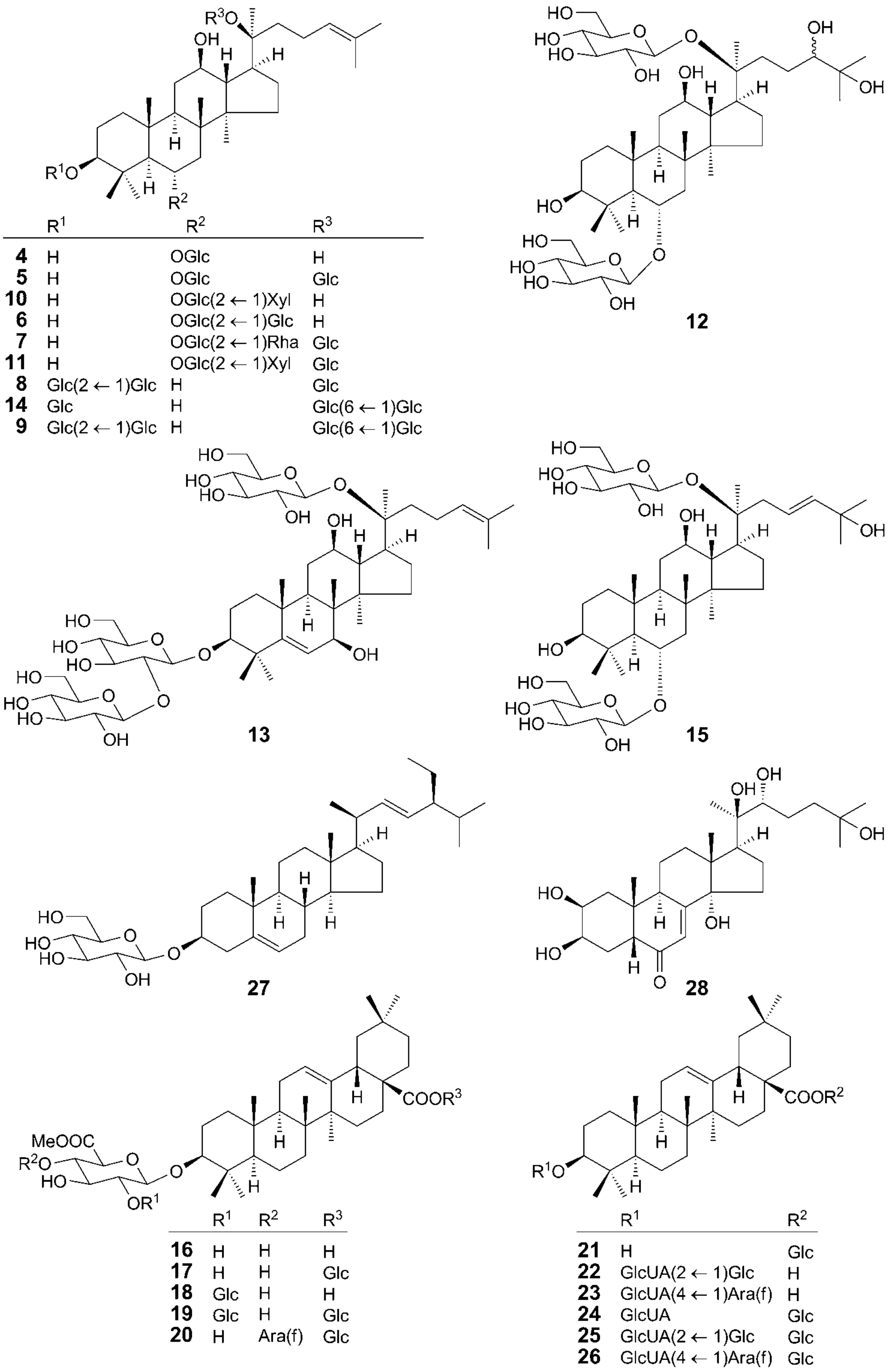
3

Fig. 1. *New compounds* **1**–**3** *isolated from the rhizomes of* P. japonicus

the known compounds **4**–**28** were identified as twelve dammarane-type triterpenoid saponins, *i.e.*, ginsenosides Rh_1 [6], Rg_1 [7], Rf [8], Re [8], Rd [9], and Rb_1 (**4**–**9**, resp.) [9], notoginsenosides R_2 [10], R_1 [10], J [11], and G (**10**–**13**, resp.) [11], gypenoside XVII (**14**) [12], and vinaginsenoside R_{15} (**15**) [13], eleven oleanane-type triterpenoid glycosides, *i.e.*, oleanolic acid 3-*O*-*β*-D-(6′-methyl ester)glucuronopyranoside [14], chikusetsusaponin IVa methyl ester [15], oleanolic acid 3-*O*-*β*-D-glucopyranosyl-(1 → 2)-*β*-D-(6′-methyl ester)glucuronopyranoside [16], chikusetsusaponin V methyl ester [5], chikusetsusaponin IV methyl ester [17], oleanolic acid 28-*O*-*β*-D-glucopyranoside [18], polysciassaponin P_5 [19], desglucosylchikusetsusaponin IV (**16**–**23**, resp.) [20], chikusetsusaponins IVa [5], V (**24** and **25**, resp.) [5], and IV (**26**) [5], one sitosterol, *β*-sitosterol 3-*O*-*β*-D-glucopyranoside (**27**) [21], and one steroid hormone, ecdysterone (**28**) [22], on the basis of spectroscopic and physicochemical comparison with authentic samples and literature data. The known saponins **12**, **15**, and **18**–**22** were reported for the first time from the title plant.

Compound **1** was obtained as a white amorphous powder. Its molecular formula was assigned as $C_{36}H_{62}O_{10}$ by HR-ESI-MS peak at *m/z* 677.4240 ($[M+Na]^+$; calc. 677.4240) and ^{13}C-NMR (DEPT) spectra. On the basis of 1D- and 2D-NMR spectral data, compound **1** was determined as (20*S*,24*Z*)-3*β*,6*α*,12*β*,20,26-pentahydroxydammar-24-ene 6-*O*-*β*-D-glucopyranoside, named yesanchinoside R_1.

The IR spectrum of **1** indicated the presence of OH group (3418 cm^{-1}). The ^1H-NMR spectrum of **1** (*Table 1*) exhibited seven Me *singlet*s at *δ*(H) 0.80 (Me(30)), 1.03 (Me(19)), 1.18 (Me(18)), 1.34 (Me(21)), 1.44 (Me(29)), 2.02 (Me(27)), and 2.12 (Me(28)), and the signals of one CH_2O group at *δ*(H) 4.56 and 4.47 (each *d*, $J = 12.0$, $CH_2(26)$), of three CH–O groups at *δ*(H) 3.52 (*dd*, $J = 11.8$, 5.0, H–C(3)), 3.96 (*ddd*, $J = 12.4$, 10.0, 4.5, H–C(12)), and 4.45 (*ddd*, $J = 12.3$, 10.0, 3.8, H–C(6)), of an olefinic H-atom at *δ*(H) 5.47 (br. *t*, $J = 6.9$, H–C(24)), as well as of an anomeric H-atom at *δ*(H) 5.06 (*d*, $J = 7.9$, H–C(1′)). In the ^{13}C-NMR and DEPT spectra of **1** (*Table 1*), 36 C-atom signals were observed, including those of seven Me, nine CH_2, including one O-



	R¹	R²	R³
4	H	OGlc	H
5	H	OGlc	Glc
10	H	OGlc(2 ← 1)Xyl	H
6	H	OGlc(2 ← 1)Glc	H
7	H	OGlc(2 ← 1)Rha	Glc
11	H	OGlc(2 ← 1)Xyl	Glc
8	Glc(2 ← 1)Glc	H	Glc
14	Glc	H	Glc(6 ← 1)Glc
9	Glc(2 ← 1)Glc	H	Glc(6 ← 1)Glc

	R¹	R²	R³
16	H	H	H
17	H	H	Glc
18	Glc	H	H
19	Glc	H	Glc
20	H	Ara(f)	Glc

	R¹	R²
21	H	Glc
22	GlcUA(2 ← 1)Glc	H
23	GlcUA(4 ← 1)Ara(f)	H
24	GlcUA	Glc
25	GlcUA(2 ← 1)Glc	Glc
26	GlcUA(4 ← 1)Ara(f)	Glc

Fig. 2. *Known compounds* **4**–**28** *isolated from the rhizomes of* P. japonicus

Table 1. *^{1}H- and ^{13}C-NMR Data of Compounds* **1** *and* **2**. At 500 and 125 MHz, respectively, in CD$_3$OD; δ in ppm, *J* in Hz.

	1		**2**	
	δ(H)	δ(C)	δ(H)	δ(C)
CH$_2$(1)	1.74 (overlapped), 1.03–0.98 (*m*, H$_\beta$)	39.7	1.68 (overlapped), 1.01–0.96 (*m*, H$_\beta$)	39.7
CH$_2$(2)	1.99–1.96 (*m*, H$_\alpha$), 1.85–1.81 (*m*, H$_\beta$)	27.9	1.93–1.90 (*m*, H$_\alpha$), 1.91–1.89 (*m*, H$_\beta$)	27.9
CH(3)	3.52 (*dd*, *J* = 11.8, 5.0)	78.7	3.55 (*dd*, *J* = 12.8, 4.8)	78.8
C(4)		40.4		40.3
CH(5)	1.45 (*d*, *J* = 10.0)	61.5	1.44 (*d*, *J* = 10.0)	61.4
CH$_2$(6)	4.45 (*ddd*, *J* = 12.3, 10.0, 3.8)	80.1	4.38 (*m*)	79.6
CH$_2$(7)	2.67 (*dd*, *J* = 12.3, 3.2, H$_\alpha$), 1.96 (*t*, *J* = 10.0, H$_\beta$)	45.3	2.46 (*dd*, *J* = 12.3, 3.2, H$_\alpha$), 1.98 (*t*, *J* = 10.0, H$_\beta$)	45.5
CH(8)		41.2		41.2
CH(9)	1.58 (*dd*, *J* = 12.5, 3.0)	50.3	1.56 (*dd*, *J* = 12.0, 2.8)	50.2
C(10)		39.6		39.6
CH$_2$(11)	2.14 (overlapped), 1.52–1.47 (*m*, H$_\beta$)	32.0	2.16 (overlapped), 1.58–1.52 (*m*, H$_\beta$)	32.0
CH(12)	3.96 (*ddd*, *J* = 12.4, 10.0, 4.5)	71.1	3.94 (*ddd*, *J* = 12.0, 10.0, 4.2)	71.2
CH(13)	2.03 (*d*, *J* = 10.0)	48.3	2.07 (*d*, *J* = 10.0)	48.3
Me(14)		51.7		51.8
CH$_2$(15)	1.61 (overlapped), 1.12–1.08 (*m*, H$_\beta$)	31.1	1.64 (overlapped), 1.17 (overlapped)	31.1
CH$_2$(16)	1.82 (overlapped), 1.39–1.35 (*m*, H$_\beta$)	26.8	1.81 (overlapped), 1.34–1.29 (*m*, H$_\beta$)	26.9
CH(17)	2.30 (*dd*, *J* = 10.0, 7.2)	54.7	2.34 (*dd*, *J* = 10.0, 7.0)	54.8
Me(18)	1.18 (*s*)	17.4	1.20 (*s*)	17.5
Me(19)	1.03 (*s*)	17.7	1.03 (*s*)	17.8
C(20)		73.0		73.2
Me(21)	1.34 (*s*)	27.1	1.42 (*s*)	27.1
CH$_2$(22)	2.05 (overlapped), 1.71–1.68 (*m*, H$_\beta$)	36.2	2.14 (overlapped), 1.75–1.69 (*m*, H$_\beta$)	36.2
CH$_2$(23)	2.73–2.68 (*m*, H$_\alpha$), 2.45 (overlapped)	22.6	2.79–2.76 (*m*, H$_\alpha$), 2.49 (overlapped)	22.6
CH(24)	5.47 (br. *t*, *J* = 6.9)	128.0	5.54 (br. *t*, *J* = 7.0)	128.2
C(25)		136.2		136.2
CH$_2$(26)	4.56 (*d*, *J* = 12.0, H$_\alpha$), 4.47 (*d*, *J* = 12.0, H$_\beta$)	60.9	4.65 (*d*, *J* = 12.0, H$_\alpha$), 4.63 (*d*, *J* = 12.0, H$_\beta$)	60.9
Me(27)	2.02 (*s*)	21.9	2.08 (*s*)	22.0
Me(28)	2.12 (*s*)	31.8	2.16 (*s*)	31.8
Me(29)	1.44 (*s*)	16.4	1.52 (*s*)	16.9
Me(30)	0.80 (*s*)	16.9	0.85 (*s*)	16.9
Glc				
CH(1′)	5.06 (*d*, *J* = 7.9)	106.1	5.02 (*d*, *J* = 7.3)	103.7
CH(2′)	4.10 (br. *t*, *J* = 7.9)	75.5	4.45–4.42 (*m*)	79.9
CH(3′)	4.32–4.30 (*m*)	79.6	4.20–4.17 (*m*)	78.8
CH(4′)	4.28–4.24 (*m*)	72.0	4.23–4.19 (*m*)	71.8
CH(5′)	4.01–3.98 (*m*)	78.2	3.88–3.85 (*m*)	78.2
CH$_2$(6′)	4.40 (*dd*, *J* = 12.0, 5.8, H$_\alpha$), 4.57 (br. *d*, *J* = 12.0, H$_\beta$)	63.2	4.36 (*dd*, *J* = 12.0, 6.0, H$_\alpha$), 4.53 (overlapped)	63.0
Xyl				
CH(1″)			5.89 (*d*, *J* = 7.0)	104.9
CH(2″)			4.26–4.23 (*m*)	75.9
CH(3″)			4.41–4.38 (*m*)	79.8
CH(4″)			4.27–4.23 (*m*)	71.3
CH$_2$(5″)			4.39 (overlapped), 3.75 (br. *t*, *J* = 11.0, H$_\beta$)	67.3

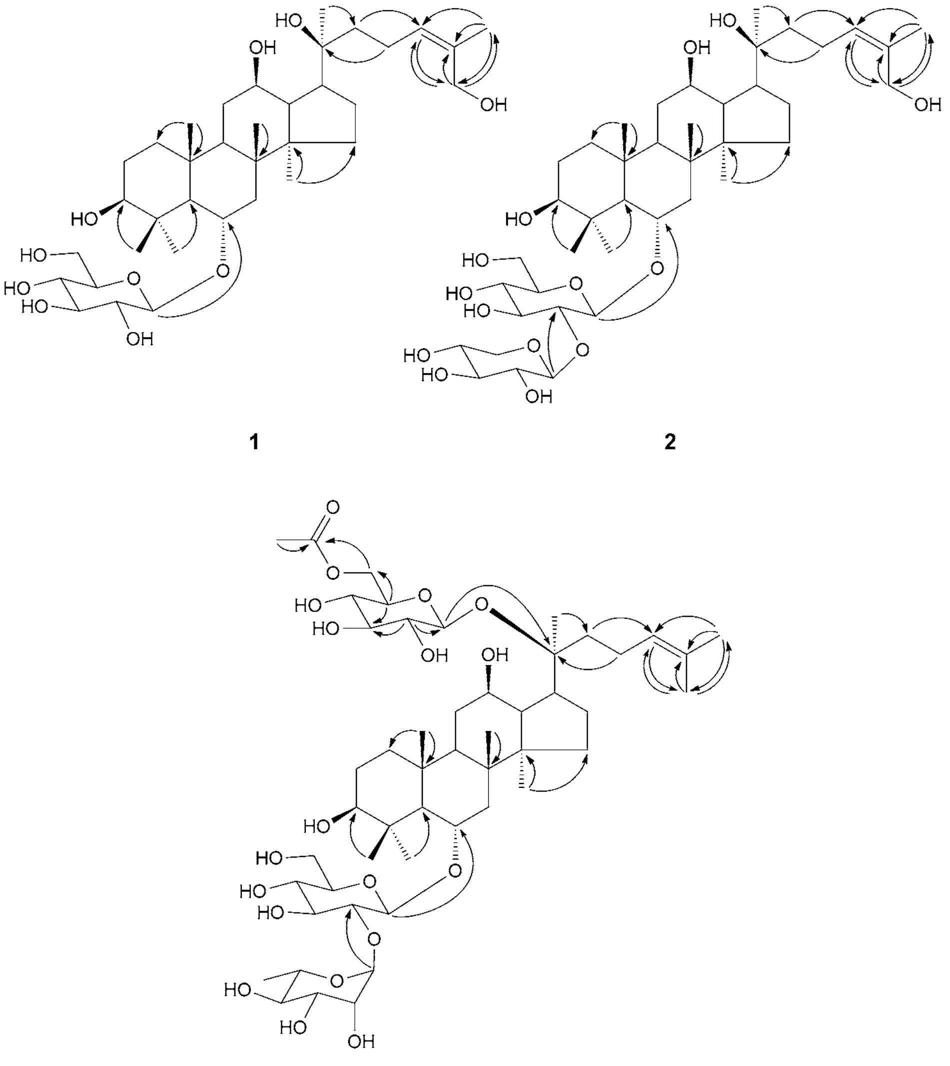
bearing one (δ(C) 60.9 (C(26))), and eight CH groups, including three O-bearing ones (δ(C) 78.7 (C(3)), 80.1 (C(6)), and 71.1 (C(12)), of six quaternary C-atoms, including one O-bearing C-atom (δ(C) 73.0 (C(20)), and a set of signals (δ(C) 106.1 (C(1′)), 79.6 (C(3′)), 78.2 (C(5′)), 75.5 (C(2′)), 72.0 (C(4′)), and 63.2 (C(6′))) attributed to a glucosyl moiety. Acidic hydrolysis of **1** afforded D-glucose as identified by gas chromatography (GC) analysis of its 1-(trimethylsilyl)-1*H*-imidazole derivative. These aforementioned data were similar to those of ginsenoside Rh_1 (**4**) [6], a known dammarane-type glycoside, which was also isolated in the current work. The main differences between **1** and **4** were the molecular weight, the absence of one Me signal and the appearance of an additional CH_2O signal in the NMR spectra of **1**. The molecular weight of **1** was 16 Da greater than that of **4**. In the ^{13}C-NMR spectrum of **1**, C(24), C(25), C(26), and C(27) were downfield-shifted to δ(C) 128.0, 136.2, 60.9, and 21.9, compared to δ(C) 125.9, 130.7, 25.8, and 17.6 for **4**. These data indicated that one of the Me group at C(26) or C(27) in **4** was oxidized to an CH_2O group in **1**. The key HMBC correlations (*Fig. 3*) of H–C(23) with C(20) and C(25), of H–C(24) with C(22) and C(27), of H–C(26) with C(24), C(25), and C(27), and of H–C(27) with C(24) and C(26) further confirmed this proposition. The configuration of the C(24)=C(25) bond was determined to be (*Z*) due to the ROESY correlation of H–C(27) with H–C(24) in **1** (*Fig. 4*). On the basis of the above evidence and the literature data [23], the structure of compound **1** was characterized as shown in *Fig. 1*.

Compound **2**, a white amorphous powder, has the molecular formula $C_{41}H_{70}O_{14}$ as deduced by HR-ESI-MS (*m*/*z* 809.4680 ($[M+Na]^+$; calc. 809.4663) and ^{13}C-NMR (DEPT) spectrum. According to 1D- and 2D-NMR data, **2** was determined as (20*S*,24*Z*)-3β,6α,12β,20,26-pentahydroxydammar-24-ene 6-*O*-β-D-xylopyranosyl-(1 → 2)-β-D-glucopyranoside, named yesanchinoside R_2.

In the IR spectrum of **2**, the absorption band at 3419 cm^{-1} indicated the presence of OH group. The ^{1}H- and ^{13}C-NMR data of **2** were closely similar to those of **1**, except for the appearance of a set of signals arising from an additional pentosyl moiety in **2**. Acid hydrolysis of **2** afforded D-glucose and D-xylose as identified by GC analysis of their 1-(trimethylsilyl)-1*H*-imidazole derivatives. The location of the additional xylosyl group was assigned as C(2′) of the glucosyl moiety in **2**, based on the HMBC correlations from δ(H) 5.89 (Xyl H–C(1″)) to 79.9 (Glc C(2′); *Fig. 3*). In addition, the HMBC correlation of δ(H) 5.02 (Glc H–C(1′)) with δ(C) 79.6 (aglycone C(6)) was also observed. The ROESY correlations between H–C(27) and H–C(24) established the configuration of the C(24)=C(25) bond as (*Z*). Accordingly, the structure of **2** was elucidated as shown in *Fig. 1*.

Compound **3**, a white amorphous powder, has the molecular formula $C_{50}H_{84}O_{19}$ as deduced by HR-ESI-MS (*m*/*z* 1011.5515 ($[M+Na]^+$; calc. 1011.5504) and ^{13}C-NMR (DEPT) spectrum. According to 1D- and 2D-NMR data, **3** was identified as (20*S*)-3β,6α,12β,20,26-pentahydroxydammar-24-ene 6-*O*-α-L-rhamnopyranosyl-(1 → 2)-β-D-glucopyranosyl-20-*O*-(6-*O*-acetyl)-β-D-glucopyranoside [6‴-*O*-acetylginsenoside Re].

The IR spectrum of **3** showed absorption bands at 3422 cm^{-1} due to OH group. The ^{13}C-NMR spectrum of **3** (*Table 2*) exhibited 30 signals for the aglycone, which were identical to those of (20*S*)-protopanaxatriol. In addition, 20 C-atom signals arising from one Ac group (δ(C) 170.9 and 20.9) and three hexosyl moieties (anomeric C-atom signals at δ(C) 101.4 (Glc C(1′)), 102.1 (Rha C(1″)), and 98.3 (Glc C(1‴))) were



1 **2**

3

Fig. 3. *Key HMBC correlations of* **1**–**3**

observed. Acid hydrolysis of **3** afforded D-glucose and L-rhamnose as identified by GC analysis of their 1-(trimethylsilyl)-1*H*-imidazole derivatives. These NMR features were similar to those of ginsenoside Re (**7**) except for the appearance of two additional signals at δ(C) 170.9 and 20.9 due to an Ac group in **3**. A difference in the chemical-shift value of Glc $C(6''')$ (δ(C) 63.2 in **7**; δ(C) 65.1 in **3**) allowed the Ac group to be placed at $C(6''')$ of Glc. This was confirmed by the HMBC correlations from δ(H) 4.99–4.65 ($CH_2(6''')$) to the C=O C-atom of the Ac group (*Fig. 3*). Moreover, the location and sequence of the sugar moieties were confirmed by the key correlations from δ(H) 5.23

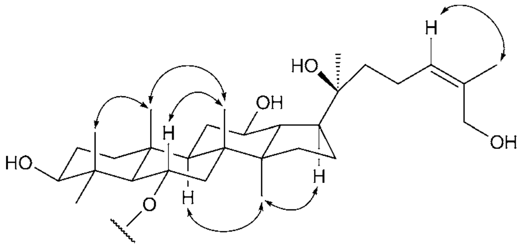


Fig. 4. *Selected ROESY correlations of* **1** and **2**

Table 2. *^{1}H- and ^{13}C-NMR Data of Compound* **3**. At 500 and 125 MHz, respectively, in C_5D_5N, δ in ppm, J in Hz.

	δ(H)	δ(C)		δ(H)	δ(C)
CH$_2$(1)	1.79 (overlapped),	39.4	CH(24)	5.18 (br. *t*, $J = 7.5$)	126.0
	1.05–1.01 (*m*, H$_\beta$)		C(25)		131.0
CH$_2$(2)	1.91–1.88 (*m*, H$_\alpha$),	27.5	Me(26)	1.58 (*s*)	25.8
	1.81–1.79 (*m*, H$_\beta$)		Me(27)	1.55 (*s*)	17.3
CH(3)	3.50 (*dd*, $J = 12.0$, 5.0)	78.3	Me(28)	2.14 (*s*)	32.2
C(4)		40.0	Me(29)	1.30 (*s*)	17.4
CH(5)	1.38–1.36 (*m*)	60.8	Me(30)	0.85 (*s*)	17.3
CH(6)	4.71 (*ddd*, $J = 12.0$, 9.8, 3.0)	74.2	Glc		
CH$_2$(7)	2.16 (*dd*, $J = 12.0$, 3.0, H$_\alpha$),	46.0	CH(1′)	5.23 (*d*, $J = 6.8$)	101.4[a])
	1.98 (*t*, $J = 10.0$, H$_\beta$)		CH(2′)	4.39–4.34 (*m*)	79.3
C(8)		41.4	CH(3′)	4.31–4.28 (*m*)	78.3
CH(9)	1.54–1.52 (*m*)	59.6	CH(4′)	4.26–4.23 (*m*)	72.4
C(10)		39.8	CH(5′)	3.96–3.92 (*m*)	78.3
CH$_2$(11)	2.14–2.11 (*m*, H$_\alpha$),	30.9	CH$_2$(6′)	4.51 (*dd*, $J = 11.8$, 5.4, H$_\alpha$),	62.9
	1.50–1.45 (overlapped)			4.36 (overlapped)	
CH(12)	4.22–4.15 (*m*)	70.3	Rha		
CH(13)	1.90 (*d*, $J = 10.0$)	49.2	CH(1″)	6.52 (br. *s*)	102.1[a])
C(14)		51.5	CH(2″)	4.81 (br. *d*, $J = 2.5$)	72.3
CH$_2$(15)	1.51–1.46 (overlapped),	30.9	CH(3″)	4.70–4.68 (*m*)	72.5
	1.05–1.01 (*m*, H$_\beta$)		CH(4″)	4.37–4.35 (*m*)	74.2
CH$_2$(16)	1.79 (overlapped),	26.8	CH(5″)	4.99–5.02 (*m*)	69.5
	1.30–1.27 (*m*, H$_\beta$)		Me(6″)	1.79 (*d*, $J = 6.5$)	18.7
CH(17)	2.48–2.42 (*m*)	51.8	Glc		
Me(18)	1.22 (*s*)	17.9	CH(1‴)	5.20 (*d*, $J = 7.8$)	98.3
Me(19)	1.01 (*s*)	17.7	CH(2‴)	4.05–4.02 (*m*)	75.2
C(20)		83.4	CH(3‴)	4.16–4.12 (*m*)	79.1
Me(21)	1.59 (*s*)	22.4	CH(4‴)	4.23–4.19 (*m*)	71.6
CH$_2$(22)	2.41–2.39 (*m*, H$_\alpha$),	36.1	CH(5‴)	4.08–4.04 (*m*)	75.3
	1.84 (overlapped)		CH$_2$(6‴)	4.99 (br. *d*, $J = 12.0$, H$_\alpha$),	65.1
CH$_2$(23)	2.51–2.47 (*m*, H$_\alpha$),	23.4		4.65 (br. *t*, $J = 12.0$, H$_\beta$)	
	2.23 (overlapped)		Ac	2.09 (*s*)	20.9, 170.9

[a]) The assignment of the ^{13}C-NMR data of C(1′) and C(1″) in 6‴-*O*-acetylginsenoside Re was revised.

(H–C(1′) of Glc) to δ(C) 74.2 (C(6)), from δ(H) 6.52 (H–C(1″) of Rha) to 79.3 (C(2′) of Glc), and from δ(H) 5.20 (H–C(1‴) of Glc) to 83.4 (C(20)). Thus, the structure of **3** was elucidated as (20*S*)-3β,6α,12β,20,26-pentahydroxydammar-24-ene 6-*O*-α-L-rhamnopyranosyl-(1 → 2)-β-D-glucopyranosyl-20-*O*-(6-*O*-acetyl)-β-D-glucopyranoside. Previously, *Teng et al.* had obtained this compound by the acylation of ginsenoside Re, which was catalyzed by *Novozyme 435* using vinyl acetate as the acyl donor [24]. *Tung et al.* also isolated it from the flower-buds of *P. ginseng* steamed at 120° for 4 h under 0.15 MPa pressure [25]. These previous literature data suggest that compound **3** might be an artifact of the isolation process. To determine whether **3** was an artificial compound or natural product, two portions of ginsenoside Re (**7**; each 5 mg) were dissolved in MeOH/H_2O/0.2% AcOH and MeOH/AcOEt/H_2O (each 2 ml), respectively, and then heated at 75° for 24 h [26]. Subsequent analysis of the two reaction solutions by TLC and HPLC showed that no reaction had occurred. Thus, ginsenoside Re appears to be stable under moderate temperature and mild acidic condition, which suggested that 6‴-*O*-acetylginsenoside Re (**3**) should be a new genuine natural product. The isolation of many acylated glycosides from the title plant further confirmed this assumption [27] [28]. The assignment of the ^{13}C-NMR data of C(1′) and C(1″) in 6‴-*O*-acetylginsenoside Re [24] was revised.

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Experimental Part

General. Column chromatography (CC): *Diaion HP-20SS* (*Mitsubishi Chemical Co.*), *MCI* gel *CHP-20P* (75–150 μm; *Mitsubishi Chemical Co.*), *RP-18* gel (40–63 μm; *Merck*), and silica gel (200–300 mesh, *Qingdao Haiyang Chemical Factory*). TLC: SiO_2 Plates; detection by spraying with 10% H_2SO_4 reagents. Optical rotations: *JASCO-20* polarimeter. IR Spectra: *Bio-Rad-FTS-135* spectrometer; KBr pellets; $\tilde{\nu}_{max}$ in cm^{-1}. 1D- and 2D-NMR spectra: *Bruker-AM-400* and *-DRX-500* spectrometers; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MS: *VG-Auto-Spec-3000* spectrometer with glycerol as matrix for FAB-MS; *API-QSTAR-Pulsar-1* spectrometer for ESI-MS and HR-ESI-MS; in *m*/*z*.

Plant Material. The fresh rhizomes of *Panax japonicus* C. A. Meyer were collected from Gaoligong Mountain, Yunnan Province, China, in May of 2008, and identified by *C.-R. Y.* A voucher specimen (KUN 0567863) has been deposited with the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The fresh rhizomes of *Panax japonicus* (18.0 kg) were extracted with MeOH (3 × 10 l) at 60° for 6 h each time. After removal of the solvent under reduced pressure, a residue (2.1 kg) was obtained. A part of this residue (1.8 kg) was dissolved in H_2O (6 l), and then extracted successively with AcOEt (4 l × 3) and BuOH (4 l × 3). The BuOH extract (1.4 kg) was chromatographed on *Diaion HP-20SS* with H_2O/MeOH 1 : 0 → 0 : 1 to give *Frs. 1–5*. *Fr. 1* (120 g) was subjected to CC (*MCI*-gel *CHP-20P*; H_2O/MeOH 1 : 0 → 7 : 3; silica gel; $CHCl_3$/MeOH 9 : 1 → 5 : 5; and *RP-18*; H_2O/MeOH 5 : 5 → 0 : 1) to yield **2** (18 mg), **8** (12 mg), **12** (15 mg), **13** (2 mg), **14** (10 mg), and **15** (4 mg). Repeated CC (*MCI* gel *CHP-20P*; H_2O/MeOH 1 : 0 → 7 : 3; silica gel; ($CHCl_3$/MeOH 9 : 1 → 5 : 5); and *RP-18*; H_2O/MeOH 5 : 5 → 0 : 1) afforded **1** (19 mg), **3** (25 mg), **7** (6.45 g), **9** (4.58 g), and **11** (12 mg) from *Fr. 2* (51 g). *Fr. 3* (30 g) was repeatedly purified by CC (*MCI*-gel *CHP-20P*; H_2O/MeOH 1 : 0 → 7 : 3; silica gel; $CHCl_3$/MeOH 8 : 2 → 5 : 5; and *RP-18*; H_2O/MeOH 5 : 5 → 0 : 1) to yield **5** (4.54 g), **6** (5 mg), **16** (15 mg), **17** (10 mg), **18** (50 mg), **19** (13 mg), **20** (34 mg), **21** (19 mg), **22** (9 mg), **23** (7.22 g), and **24** (580 mg). Similarly, *Fr. 4* (5.5 g) was subjected to CC (*MCI* gel *CHP-20P*; H_2O/MeOH 1 : 0 → 3 : 7; *RP-*

18; H_2O/MeOH 5:5 → 0:1, and silica gel; $CHCl_3$/MeOH 8.5:1.5 → 6:4) to give **25** (115 mg) and **26** (30 mg). Compounds **4** (12 mg) and **10** (20 mg) were obtained from *Fr. 5* (3.0 g) by repeated CC (*MCI*-gel *CHP-20P*; H_2O/MeOH 1:0 → 7:3; silica gel; $CHCl_3$/MeOH 9:1 → 5:5; and *RP-18*; H_2O/MeOH 5:5 → 0:1).

The AcOEt extract (25 g) was subjected to CC (*MCI* gel *CHP-20P;* H_2O/MeOH 1:0 → 1:0) to give five fractions, *Frs. E1 – E5*. *Fr. E1* (12 g) was further purified by CC (silica gel; $CHCl_3$/MeOH 20:1 → 7:3; and *RP-18*; H_2O/MeOH 5:5 → 0:1) to afford **27** (19 mg) and **28** (18 mg).

Yesanchinoside R₁ (*=(3β,5α,6α,12β,17β)-17-[(1*S*,4*Z*)-1,6-Dihydroxy-1,5-dimethylhex-4-en-1-yl]-3,12-dihydroxy-8,10,14-trimethylgonan-6-yl β-*D*-Glucopyranoside*; **1**). White amorphous powder. $[\alpha]_{\mathrm{D}}^{27} = +12.6$ ($c = 0.10$, MeOH). IR: 3418, 2964, 2876, 1638, 1460, 1377, 1077, 1029. ^{1}H- and ^{13}C-NMR: *Table 1*. ESI-MS (pos.): 677 ($[M+\mathrm{Na}]^+$). HR-ESI-MS (pos.): 677.4240 ($[M+\mathrm{Na}]^+$, $C_{36}H_{62}NaO_{10}^+$; calc. 677.4240).

Yesanchinoside R₂ (*=(3β,5α,6α,12β,17β)-17-[(1*S*,4*Z*)-1,6-Dihydroxy-1,5-dimethylhex-4-en-1-yl]-3,12-dihydroxy-8,10,14-trimethylgonan-6-yl 2-*O*-β-*D*-Xylopyranosyl-β-*D*-glucopyranoside*; **2**). White amorphous powder. $[\alpha]_{\mathrm{D}}^{27} = -4.92$ ($c = 0.11$, MeOH). IR: 3419, 2942, 2879, 1738, 1640, 1455, 1388, 1077.^{1}H- and ^{13}C-NMR: *Table 1*. ESI-MS (pos.): 809 ($[M+\mathrm{Na}]^+$). HR-ESI-MS (pos.): 809.4680 ($[M+\mathrm{Na}]^+$, $C_{41}H_{70}NaO_{14}^+$; calc. 809.4663).

*6'''-*O*-Acetylginsenoside Re* (*=(3β,6α,12β)-20-[(6-*O*-Acetyl-β-*D*-glucopyranosyl)oxy]-3,12-dihydroxydammar-24-en-6-yl 2-*O*-(6-Deoxy-α-*L*-mannopyranosyl)-β-*D*-glucopyranoside*; **3**). White amorphous powder. $[\alpha]_{\mathrm{D}}^{27} = -4.8$ ($c = 0.14$, MeOH). IR: 3422, 2933, 2878, 1742, 1647, 1457, 1371, 1043. ^{1}H- and ^{13}C-NMR: *Table 2*. ESI-MS (pos.): 1011 ($[M+\mathrm{Na}]^+$). HR-ESI-MS (pos.): 1011.5515 ($[M+\mathrm{Na}]^+$, $C_{50}H_{84}NaO_{19}^+$; calc. 1011.5504).

Assay for Determining whether **3** *Was an Artifact or Natural Product.* Two portions of ginsenoside Re (**7**; each 5 mg) were dissolved in MeOH/H_2O/0.2% AcOH and MeOH/AcOEt/H_2O (each 2 ml), resp., and then, heated at 75° for 24 h. The reaction process was monitored by TLC and HPLC [26].

Acid Hydrolysis of Compounds **1**–**3**. Compounds **1**–**3** (each 4.0 mg) were hydrolyzed with 2N HCl/1,4-dioxane 1:1 (4 ml) at 80° for 8 h. The mixture was extracted with $CHCl_3$ (3×4 ml). The aq. layer was neutralized with *Amberlite IRA-401*, and the resin was removed by filtration. The filtrate was evaporated to dryness, and the resulting monosaccharides were dissolved in pyridine (2 ml). Then, L-cysteine methyl ester hydrochloride (1.5 mg) was added. After heating at 60° for 1 h, 1-(trimethylsilyl)-1*H*-imidazole (1.5 ml) was added. The mixture was heated at 60° for another 30 min. An aliquot (4 μl) of the supernatant was removed and directly subjected to GC analysis: column temp., 180–280° at 3 deg/min; carrier gas, N_2 (1 ml/min), injector and detector temp., 250°; split ratio, 1:50. The configurations of monosaccharides were determined by comparison of the retentions times (t_{R} values) of the corresponding derivatives with those of authentic samples. The GC (t_{R} values) of the D-glucose, D-xylose, and L-rhamnose derivatives were 19.450, 14.283, and 15.912 min, resp.

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