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OLEANANE AND URSANE GLYCOSIDES FROM *SCHEFFLERA OCTOPHYLLA*

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Key Word Index—*Schefflera octophylla*; Araliaceae; triterpene glycoside; oleanane; ursane; asiaticoside; cauloside D; scheffoleoside A, B, D, E, F; scheffursoside B, C, D, E, F.

Abstract—Twelve triterpene glycosides were isolated from the bark of *Schefflera octophylla* of Vietnamese origin. Three of them were identified as asiaticoside, cauloside D and 3α-hydroxyurs-12-ene-23,28-dioic acid 28-*O*-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranoside. The structures of nine new glycosides were elucidated by chemical and spectroscopic evidence. Including the known compounds, the 12 glycosides consisted of six pairs of corresponding ursene and oleanene glycosides and all of them had the same triose moiety at the C-28 position. The names scheffurosides A–F and scheffoleosides B–F were proposed for corresponding pairs of ursene and oleanene glycosides, respectively.

INTRODUCTION

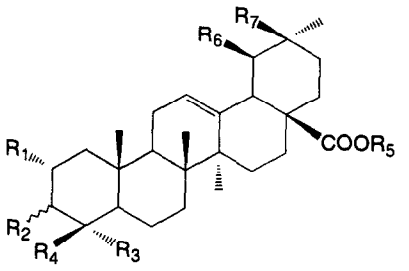
The South Asian plant, *Schefflera octophylla* (Lour.) Harm is used as a folk remedy in Vietnam as a tonic, antipyretic, anti-inflammatory and analgesic. Previous studies on the constituents of leaves of this plant revealed the isolation of 10 lupane type triterpenes, all of which have a 28-COOH group [1–7]. From the bark of this plant, long chain fatty acid esters of 3α-hydroxylup-20(29)-ene-23,28-dioic acid and two ursane glycosides, asiaticoside (**1**) and 3α-hydroxyurs-12-ene-23,28-dioic acid 28-*O*-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranoside (**7**) [8, 9] were isolated.

In the present study, we describe the isolation and characterization of nine new glycosides together with the identification of known glycosides, **1**, **6** and **7**.

RESULTS AND DISCUSSION

From the MeOH extract of the bark of *S. octophylla* followed by Diaion, silica gel chromatography and HPLC, 12 compounds (**1**–**12**) were isolated.

Compound **1** ($C_{48}H_{78}O_{19}$) was identified as asiaticoside by comparison of ^{1}H NMR and ^{13}C NMR data (Table 1) with those of the authentic compound isolated from the same plant [9], as well as *Centella asiatica* (Umbelliferae) [10].



Compound **2** had the same molecular formula as **1**. The ^{13}C NMR data measured in pyridine-d_5 (Table 1) was essentially the same as those of **1** for A–B rings and the triose moiety. In the ^{1}H NMR data, six singlet methyl signals were observed, and an olefinic proton signal at δ5.42 (1H, broad *s*, H-12) and a signal δ3.17 (1H, *dd*, *J* = 3.5 and 9.9 Hz, H-18) were characteristic for olean-12-en-28-oic acid derivatives. On acid hydrolysis, glucose and rhamnose were detected. The FAB-MS (negative) spectra of **2** showed ions at *m/z* 957 $[M-H]^-$, 811 $[M-Rha]^-$, 649 $[M-Rha-Glc]^-$ and 487 $[M-Rha-Glc-Glc]^-$. When the ^{13}C NMR spectrum of **2** was compared with that of papyrioside L-IIc (oleanolic acid 28-*O*-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl (1→6)-β-D-glucopyranoside) [11], all signals due to triose carbons were essentially the same. Also, the ^{13}C NMR signals of C, D and E ring carbons of the aglycone moiety were almost superimposable with those of **6** (see below).

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urs-12-ene	R_1	R_2	R_3	R_4	R_5	R_6	R_7
1	OH	β-OH	CH_2OH	CH_3	Glc^6 Glc^4Rha	CH_3	H
1a	OH	β-OH	CH_2OH	CH_3	H	CH_3	H
3	OH	β-OH	CHO	CH_3	Glc^6 Glc^4Rha	CH_3	H
3a	OH	β-OH	CHO	CH_3	H	CH_3	H
5	H	β-O-Ara	CH_2OH	CH_3	Glc^6 Glc^4Rha	CH_3	H
7	H	α-OH	COOH	CH_3	Glc^6 Glc^4Rha	CH_3	H
9	H	β-O-$GlcA^2$ Gal^2Glc	CH_3	CH_3	Glc^6 Glc^4Rha	CH_3	H
9p	H	β-O-$GlcA^2$ Gal^2Glc	CH_3	CH_3	H	CH_3	H
11	OH	β-OH	CH_3	CH_2OH	Glc^6 Glc^4Rha	CH_3	H
The corresponding olean-12-ene							
2	OH	β-OH	CH_2OH	CH_3	Glc^6 Glc^4Rha	H	CH_3
4	OH	β-OH	CHO	CH_3	Glc^6 Glc^4Rha	H	CH_3
6	H	β-O-Ara	CH_2OH	CH_3	Glc^6 Glc^4Rha	H	CH_3
8	H	α-OH	COOH	CH_3	Glc^6 Glc^4Rha	H	CH_3
10	H	β-O-$GlcA^2$ Gal^2Glc	CH_3	CH_3	Glc^6 Glc^4Rha	H	CH_3
12	OH	β-OH	CH_3	CH_2OH	Glc^6 Glc^4Rha	H	CH_3
13	OH	β-OH	CH_3	CH_2OH	H	H	CH_3

Glc ; β-D-glucopyranosyl, Rha ; α-L-rhamnopyranosyl, Ara ; α-L-arabinopyranosyl
Gal ; β-D-galactopyranosyl, GlcA ; β-D-glucuronopyranosyl

Table 1. ^{13}C NMR spectral data of **1–12** (pyridine-d_5, 100 MHz)

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9***	**10***	**11**	**12**
C- 1	47.8	47.7	47.9	48.1	39.0	38.9	32.9	32.8	38.8	38.7	48.0	47.8
2	68.9	68.9	68.1	68.1	26.2	26.1	26.0	26.0	26.1	26.2	68.7	68.7
3	78.1	78.2	78.0	78.0	82.0	82.0	72.9	72.9	90.6	90.1	85.7	85.7
4	43.6	43.6	56.6	56.6	43.5	43.5	51.8	51.8	39.4	39.5	44.0	44.0
5	48.1	48.2	48.0	47.6	47.6	47.7	44.7	44.9	55.7	55.8	56.5	56.5
6	18.4	18.6	20.6	20.7	18.2	18.2	21.8	21.8	18.3	18.4	18.5	18.6
7	33.1	32.8	32.8	32.5	33.2	32.8	33.4	33.1	33.1	33.1	33.8	33.4
8	40.2	40.0	40.2	40.0	40.2	40.0	40.7	40.5	39.8	39.7	40.2	40.0
9	48.0	48.0	48.0	48.1	48.1	48.2	48.2	48.2	47.7	47.8	48.2	48.3
10	38.3	38.4	38.3	38.4	36.9	37.0	37.2	37.3	36.5	36.8	38.3	38.4
11	23.8	23.3	23.8	23.3	23.8	23.4	23.6	23.4	23.5	23.3	24.0	23.4
12	126.0	122.8	125.7	122.6	126.1	123.0	126.0	123.0	126.1	122.9	125.9	122.7
13	138.5	144.2	138.6	144.2	138.5	144.1	138.6	144.3	138.1	144.0	138.5	144.2
14	42.5	42.2	42.6	42.2	42.5	42.2	42.7	42.3	42.3	42.0	42.5	42.1
15	28.7	28.2	28.6	28.2	28.8	28.3	28.7	28.3	28.5	28.2	28.7	28.2
16	24.5	24.0	24.6	23.9	24.6	23.9	24.6	23.8	24.4	23.7	24.6	24.2
17	48.4	47.0	48.4	47.0	48.4	47.0	48.4	47.1	48.5	47.0	48.4	47.1
18	53.2	41.6	53.2	41.7	53.3	41.7	53.3	41.7	53.0	41.6	53.2	41.7
19	39.3	46.2	39.3	46.2	39.4	46.2	39.3	46.2	39.2	46.2	39.4	46.2
20	39.0	30.7	39.0	30.8	39.1	30.8	39.1	30.7	39.4	30.6	39.1	30.8
21	30.8	34.0	30.8	34.0	30.8	34.0	30.8	34.0	30.5	33.9	30.8	34.0
22	36.8	32.5	36.8	32.5	36.9	32.6	36.8	32.6	36.6	32.4	36.9	32.6
23	66.4	66.5	206.5	206.5	64.5	64.6	179.6	179.6	27.9	28.1	24.2	24.2
24	14.3	14.3	10.7	10.7	13.7	13.6	18.2	18.2	16.6	16.8	65.7	65.7
25	17.6	17.5	17.3	17.2	16.4	16.2	16.2	16.0	15.5	15.5	17.6	17.5
26	17.8	17.6	17.4	17.5	17.8	17.6	18.0	17.9	17.4	17.4	17.6	17.4
27	23.7	26.0	23.8	26.1	23.8	26.0	23.6	26.0	23.6	26.0	23.8	26.1
28	176.3	176.5	176.3	176.5	176.3	176.5	176.3	176.6	176.0	175.8	176.3	176.5
29	17.3	33.1	17.7	33.1	17.4	33.1	17.3	33.1	17.2	33.1	17.4	33.1
30	21.3	23.7	21.3	23.7	21.3	23.7	21.2	23.7	21.2	23.6	21.3	23.7

Table 1. *Continued*

		1	2	3	4	5	6	7	8	9*	10*	11	12
28-*O*-sugar													
Glc-	1	95.6	95.6	95.6	95.7	95.6	95.7	95.6	95.7	95.1	95.4	95.7	95.7
(inner)	2	73.9	73.9	74.0	74.0	74.0	74.0	73.7	73.8	74.4	74.4	73.8	73.9
	3	77.9	78.0	77.1	77.1	78.0	78.1	77.9	78.0	77.2	77.9	78.0	78.1
	4	70.9	70.8	71.0	70.8	71.0	70.9	71.0	70.9	70.1	70.4	71.0	70.9
	5	77.1	77.1	77.2	77.2	77.2	77.2	77.1	77.2	77.1	77.1	77.2	77.2
	6	69.3	69.2	69.4	69.2	69.5	69.2	69.4	69.2	69.0	69.0	69.5	69.3
Glc-	1	104.8	104.8	105.0	104.9	105.0	104.9	105.0	104.9	105.0	105.9	105.0	104.9
(middle)	2	75.3	75.3	75.3	75.3	75.4	75.4	75.3	75.3	73.9	74.8	75.4	75.4
	3	76.4	76.5	76.5	76.5	76.6	76.6	76.5	76.5	76.6	76.6	76.6	76.5
	4	78.6	78.7	78.7	78.7	78.8	78.8	78.7	78.8	78.2	78.5	78.8	78.8
	5	78.2	78.3	78.3	78.3	78.3	78.3	78.2	78.3	77.8	78.4	78.3	78.3
	6	61.3	61.3	61.4	61.3	61.4	61.3	61.3	61.3	60.9	61.0	61.4	61.3
Rha-	1	102.6	102.7	102.7	102.8	102.7	102.8	102.7	102.8	101.9	102.4	102.7	102.8
(terminal)	2	72.5	72.5	72.6	72.6	72.6	72.6	72.5	72.6	71.5	72.1	72.6	72.6
	3	72.7	72.7	72.8	72.8	72.8	72.8	72.8	72.8	72.1	72.3	72.8	72.8
	4	73.7	73.8	73.8	73.9	73.8	73.8	74.0	74.0	72.9	73.4	74.0	74.0
	5	70.2	70.3	70.3	70.3	70.3	70.3	70.3	70.3	70.0	70.2	70.3	70.3
	6	18.4	18.5	18.5	18.5	18.5	18.5	18.5	18.5	17.8	18.2	18.5	18.6
3-*O*-sugar													
Ara/GlcA	1				(Ara)	106.7	106.7		(GlcA)	103.8	104.2		
(inner)	2					73.1	73.1			82.0	82.9		
	3					74.6	74.8			76.1	76.3		
	4					69.6	69.6			71.5	72.3		
	5					67.0	67.0			75.6	75.9		
	6									177.2	176.9		
Gal-	1									103.3	103.9		
(middle)	2									82.3	83.4		
	3									75.3	76.1		
	4									68.7	68.8		
	5									76.0	76.2		
	6									61.6	61.7		
Glc-	1									104.0	104.4		
(terminal)	2									75.6	76.2		
	3									77.0	77.5		
	4									69.9	70.4		
	5									77.0	77.6		
	6									61.5	61.6		

*Measured in the mixture of pyridine-d_5 and D_2O.

Thus the new glycoside **2** was 2α,3β,23-trihydroxyolean-12-en-28-oic acid 28-*O*-α-L-rhamnopyranosyl (1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranoside. The name, scheffoleoside A is proposed for **2**. The aglycone of **2**, arjunolic acid (**2a**) has been isolated from *Terminalia arjuna* (Combretaceae) [12].

Compound **3**, $C_{48}H_{76}O_{19}$, was a similar triterpene glycoside, and its ^{1}H NMR spectrum showed signals at δ2.50 (1H, *d*, *J* = 11.5 Hz, H-18), 5.42 (1H, broad *s*, H-12), 0.91 (3H, *d*, *J* = 7.1 Hz) and 0.93 (3H, *d*, *J* = 6.4 Hz), H-29 and H-30, which are characteristic of urs-12-en-28-oic acid. The anomeric carbon signals (Table 1) indicated the presence of three sugar units with an ester bond (δ95.6). Acid hydrolysis of **3** yielded glucose and rhamnose. FAB-MS (negative) of **3** showed ions at *m/z* 955 $[M-H]^-$, 809 $[M-Rha]^-$, 647 $[M-Rha-Glc]^-$ and 485 $[M-Rha-Glc-Glc]^-$. In the ^{13}C NMR spectrum of **3**, an aldehyde carbon signal (δ206.5) was observed and the spectrum was very similar to that of **1**, except for the A-ring carbon signals. Enzymatic hydrolysis of **3** by crude hesperidinase afforded the aglycone (**3a**), and its ^{1}H NMR spectrum showed the presence of 2α- and 3β-hydroxy groups [δ4.23 (1H, *ddd*, *J* = 4.6, 9.4 and 13.8 Hz) and 4.04 (1H, *d*, *J* = 9.4 Hz)], respectively. Hydrogenation of **3a** with $NaBH_4$ afforded asiatic acid (**1a**), the aglycone of **1**. Thus the structure of **3a** was characterized as 2α,3β-dihydroxy-23-oxo-urs-12-en-28-oic acid. When the ^{13}C NMR spectra of **3** and **3a** were compared, a glycosylation shift was observed for C-28, and the triose signals of **3** were almost superimposable with those of **1**. It

follows that **3** can be formulated as 2α,3β-dihydroxy-23-oxo-urs-12-en-28-oic acid 28-*O*-α-L-rhamnopyranosyl (1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranoside, and named scheffursoside **B**.

Compound **4**, $C_{48}H_{76}O_{19}$ was also a similar triterpene trioside having an aldehyde group (δ_C 206.5), and six singlet methyl proton signals suggested an oleanane skeleton. The FAB-MS pattern and the sugars obtained by acid hydrolysis were the same as those of **3**. On comparison of the ^{13}C NMR data (Table 1) with those of **2** and **3**, the structure of **4** was decided to be 2α,3β-dihydroxy-23-oxo-olean-12-en-28-oic acid 28-*O*-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranoside, and named scheffoleoside B. It should be noted that the relationship of **3** and **4** are the same as that of **1** and **2**, namely, the difference between them is due to the disposition of the methyl groups on the E-ring only.

Compound **6** was a similar oleanane triterpene glycoside with four monosaccharide units as deduced from the ^{13}C NMR spectrum. Acid hydrolysis of **6** yielded glucose, rhamnose and arabinose. The carbon signals assignable to the aglycone moiety were similar to those of hederagenin, but with glycosylation shifts around C-3 and C-28. By matching their NMR data, **6** was identified as Kizuta saponin K_{10} [13], a constituent of *Hedera rhombea* of the same family, which was previously isolated from *Caulophyllum robustum* (Berberidaceae) and named cauloside D [14].

Compound **5**, $C_{53}H_{86}O_{22}$ has the same molecular formula as **6** and the aglycone moiety showed the typical NMR signals for urs-12-en-28-oic acid. The results from acid hydrolysis and the FAB-MS were the same as those for **6**. On comparison of the ^{13}C NMR data of **5** (Table 1) with those of **1** while **6**, the signals due to the C–E rings and the esterified triose moiety were in good agreement with those of **1**, and those of the A–B rings, and arabinosyl carbons were almost superimposable with those of **6**. It followed that **5** can be formulated as 3-*O*-α-L-arabinopyranosyl hederagenin 28-*O*-α-L-rhamnopyranosyl (1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranosyl ester, and named scheffursoside C.

Compound **7** was similar to urs-12-en-28-oic acid ester trioside, and was identified as 3α-hydroxy-urs-12-ene-23,28-dioic acid 28-*O*-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranoside, previously isolated from the same species [9]. The trivial name, scheffursoside D is proposed for **7**.

Compound **8** has the same molecular formula, $C_{48}H_{76}O_{19}$ as **7**, yielded the same constituent monosaccharides as **2** on acid hydrolysis, and the FAB-MS pattern due to stepwise cleavage of the sugar moiety was similar to that of **7**. The ^{13}C NMR signals of **8** can be explained by the combination of the A–B rings of **7** and C–E rings and triosyl unit of **6** (Table 1). Thus, **8** is 3α-hydroxy-olean-12-ene-23,28-dioic acid 28-*O*-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranoside, and named scheffoleoside D.

Compounds **9** and **10** had the same molecular formula, $C_{66}H_{106}O_{33}$ (HR-FAB-MS). The comparison of the ^{13}C NMR signals with reported data [15, 16] revealed that **9** and **10** were bisdesmosides of ursolic acid and oleanolic acid, respectively. On acid hydrolysis, **9** yielded glucuronic acid, galactose, glucose and rhamnose. On comparison of the ^{13}C NMR spectrum of **9** with that of ursolic acid, a significant glycosylation shift was observed around C-3 and C-28. Selective degradation of the ester sugar chain [15] afforded a prosapogenin (**9p**) and methylated oligosaccharide (**9s**). The structure of **9s** was the same as the methyl trioside (a mixture of α and β-anomers of methyl α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranoside) obtained from huzhangoside B by the same degradative reaction [15]. The monodesmosidic prosapogenin (**9p**), $C_{48}H_{76}O_{19}$ was 3-*O*-glycoside of ursolic acid and showed three anomeric carbon signals (δ106.5, 105.1, 104.4) in the ^{13}C NMR spectrum. On acid hydrolysis, **9p** afforded glucose, glucuronic acid and galactose. To decide the sequence of the sugar chain, **9p** was acetylated and methylated to give **9pa**.

The mass spectrum of **9pa** exhibited fragment ions at *m/z* 331 [(hexose)Ac_4], 619 [(hexose–hexose)Ac_7] and 893 [(methyl glucuronate–hexose–hexose)Ac_9], indicating that the sugar chain was a linear triose with glucuronic acid as the inner unit. All sugar protons were assigned by H–H COSY (Experimental), and the NOESY of **9pa** exhibited cross peaks between H-3 of aglycone (δ3.17) and H-1 of glucuronic acid (δ4.65), between H-2 of glucuronic acid (δ3.82) and H-1 of galactose (δ4.60), and between H-2 of galactose (δ3.62) and H-1 of glucose (δ4.55). It followed that **9p** must be assigned as 3-*O*-β-D-glucopyranosyl(1→2)-β-D-galactopyranosyl(1→2)-β-D-glucuronopyranosyl urs-12-en-28-oic acid. The sequence of the sugar moieties of **9pa** was verified by the fact that the chemical shift values of H-2 of glucuronic acid and galactose were significantly displaced upfield more than those of the protons at acetylated positions. Consequently, the structure of bisdesmoside **9** was represented as 3-*O*-β-D-glucopyranosyl(1→2)-β-D-galactopyranosyl (1→2)-β-D-glucuronopyranosyl urs-12-en-28-oic acid 28-*O*-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl (1→6)-β-D-glucopyranosyl ester, and named scheffursoside E.

Compound **10** exhibited the same ^{13}C NMR pattern as that of **9** for the sugar moiety and the A–D ring carbons, while the E-ring carbon signals were almost the same as those of oleanolic acid. Therefore **10** was the corresponding oleanane derivative of **9** and represented as 3-*O*-β-D-glucopyranosyl(1→2)-β-D-galactopyranosyl(1→2)-β-D-glucuronopyranosyl olean-12-en-28-oic acid 28-*O*-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranosyl ester, and named scheffoleoside E.

Compounds **11** and **12** had the same molecular formula, $C_{48}H_{78}O_{19}$ (HR-FAB-MS). The comparison of the ^{13}C NMR signals of both compounds revealed that **11** and **12** were monodesmosides of ursolic acid and oleanolic acid derivatives, respectively. On acid hydrolysis, both **11** and **12** yielded galactose, glucose and rhamnose. The ^{13}C NMR spectral data of the C–E rings and the sugar moieties of **11** and **12** were essentially the same as those of **1** and **2**, respectively, while the ^{13}C NMR signals

of the other moiety (A and B rings) of **11** and **12** were essentially the same as those of the glucosyl ester of hyptatic acid B (**13**) isolated from *Hyptis capitata* (Labiatae) [16]. It follows that **11** and **12** can be formulated as 2α,3β,24-trihydroxyurs-12-en-28-oic acid 28-*O*-α-L-rhamnopyranosyl(1 → 4)-β-D-glucopyranosyl(1 → 6)-β-D-glucopyranoside, and 2α,3β,24-trihydroxyolean-12-en-28-oic acid 28-*O*-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranoside, and named scheffursoside F and scheffoleoside F, respectively.

Araliaceae plants contain many triterpene saponins of various aglycone types. Although the oleanane skeleton occurs frequently, the ursane type is very rare. It should be noted that the isolated saponins were pairs of corresponding ursane and oleanane derivatives and all of them contain the same esterified triose at the C-28 position.

EXPERIMENTAL

^{1}H NMR and ^{13}C NMR (in C_5D_5N unless otherwise stated, with TMS as int. standard): 400 and 100 MHz, respectively.

Plant material. A voucher specimen was deposited in the Herbarium of The Science Production Centre of Vietnamese Ginseng, Ho Chi Minh City University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam.

Extraction and isolation. The dried bark of *S. octophylla* (1.2 kg) was extracted with hot MeOH. After removal of the solvent by evapn, the MeOH extracts were chromatographed on highly porous polymer, DIAION HP-20 (Mitsubishi Chem. Ind. Tokyo) (H_2O, 10% MeOH and MeOH successively and finally Me_2CO). The MeOH eluate (120 g) was sepd on silica gel ($CHCl_3$–MeOH–H_2O, 30:20:1, 30:20:2, 30:20:5) to give 3 frs, A–C. Fr. A was sepd by reversed phase CC on ODS-AM 120-S50 (YMC) (50% MeOH) and then by repeated reversed phase HPLC (Merck) (65% MeOH and MeOH–0.05% TFA, 65:35) to give **1** (0.04% yield), **2** (0.014% yield), **3** (0.007% yield), **4** (0.002% yield), **11** (0.002% yield) and **12** (0.003% yield). Fr. B was sepd by reversed phase CC on ODS-AM 120-S50 (YMC) (57.5% MeOH) and then by repeated reversed phase HPLC (Merck) (60% MeOH and MeOH–0.05% TFA, 60:40) to give **5** (0.002% yield), **6** (0.002% yield), **7** (0.18% yield) and **8** (0.027% yield). Fr. C was sepd by reversed phase CC on LiChroprep RP-8 (Merck) (50% MeOH) and then by reversed phase HPLC (YMC) (45% MeOH) to give **9** (0.013% yield) and **10** (0.019% yield).

Asiaticoside (**1**). Powder, $[\alpha]_D^{16}$ −6.0° (MeOH; *c* 0.50). ^{1}H NMR: δ0.87 (3H, *d*, *J* = 6.6 Hz), 0.89 (3H, *d*, *J* = 6.4 Hz), 1.04, 1.07, 1.10, 1.16 (each 3H, *s*), 1.67 (3H, *d*, *J* = 5.9 Hz, Me of Rha), 2.47 (1H, *d*, *J* = 10.8 Hz, H-18), 3.66 (1H, *d*, *J* = 11.7 Hz, H-3), 4.96 (1H, *d*, *J* = 7.3 Hz, H-1 of Glc), 5.40 (1H, *br s*, H-12), 5.81 (1H, *br s*, H-1 of Rha), 6.15 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc); ^{13}C NMR: see Table 1.

Scheffoleoside A (**2**). Powder, negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 957.5054 $C_{48}H_{77}O_{19}$ requires 957.5059. $[\alpha]_D^{17}$ −1.4° (pyridine, *c* 1.0), ^{1}H NMR: δ0.86, 0.88, 1.08, 1.12, 1.14, 1.14 (each 3H, *s*), 1.71 (3H, *d*, *J* = 5.9 Hz, Me of Rha), 3.17 (1H, *dd*, *J* = 3.5, 9.9 Hz, H-18), 5.42 (1H, *br s*, H-12), 5.86 (1H, *br s*, H-1 of Rha), 6.24 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc); ^{13}C NMR: see Table 1.

Scheffursoside B (**3**). Powder, negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 955.4948 $C_{48}H_{75}O_{19}$ requires 955.4902. $[\alpha]_D^{17}$ −4.7° (pyridine; *c* 0.86). ^{1}H NMR: δ0.91 (3H, *d*, *J* = 7.1 Hz), 0.93 (3H, *d*, *J* = 6.4 Hz), 1.07, 1.12, 1.15, 1.43 (each 3H, *s*), 1.70 (3H, *d*, *J* = 6.2 Hz, Me of Rha), 2.50 (1H, *d*, *J* = 11.5 Hz, H-18), 4.98 (1H, *d*, *J* = 7.3 Hz, H-1 of Glc), 5.42 (1H, *br s*, H-12), 5.85 (1H, *br s*, H-1 of Rha), 6.17 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc), 9.63 (1H, *s*, –CHO); ^{13}C NMR: see Table 1.

Enzymatic hydrolysis of **3**. A soln of **3** (13 mg) and crude hesperidinase (20 mg; Tanabe, Osaka, Japan) in H_2O (10 ml) was incubated at 37° for 24 hr. The hydrolysate was extracted with $CHCl_3$, affording **3a** (6 mg).

Compound **3a**. Powder, negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 485.3302 $C_{30}H_{45}O_5$ requires 485.3267. $[\alpha]_D^{16}$ +26.7° (pyridine; *c* 0.3). ^{1}H NMR: δ0.96 (3H, *d*, *J* = 6.2 Hz), 0.99 (3H, *d*, *J* = 6.4 Hz), 1.01, 1.02, 1.21, 1.43 (each 3H, *s*), 2.63 (1H, *d*, *J* = 11.2 Hz, H-18), 4.04 (1H, *d*, *J* = 9.4 Hz, H-3), 4.23 (1H, *ddd*, *J* = 4.6, 9.4, 13.8 Hz, H-2), 5.47 (1H, *br s*, H-12), 9.65 (1H, *s*, –CHO); ^{13}C NMR: δ47.8 (C-1), 68.1 (C-2), 77.1 (C-3), 56.6 (C-4), 48.0 (C-5), 20.6 (C-6), 32.8 (C-7), 40.1 (C-8), 48.0 (C-9), 38.3 (C-10), 23.7 (C-11), 125.3 (C-12), 139.4 (C-13), 42.6 (C-14), 28.6 (C-15), 24.9 (C-16), 48.1 (C-17), 53.5 (C-18), 39.4 (C-19), 39.5 (C-20), 31.1 (C-21), 37.4 (C-22), 206.5 (C-23), 10.8 (C-24), 17.2 (C-25), 17.4 (C-26), 23.9 (C-27), 179.9 (C-28), 17.5 (C-29), 21.4 (C-30).

Reduction of **3a** *with* $NaBH_4$. To a soln of **3a** (4.5 mg) in EtOH (2 ml), $NaBH_4$ (20 mg) was added and the mixt. was reacted at room temp. for 12 hr. The reaction mixt. was acidified by passing it through Dowex 50W-X8 (H^+ form) to give a powder, which was identified by comparison of ^{1}H NMR and ^{13}C NMR spectra with those of corresponding authentic sample (**1a**).

Compound **1a**. Negative ion FAB-MS: *m/z* 487 $[M-H]^-$. $[\alpha]_D^{16}$ +13.8° (MeOH; *c* 0.48), ^{13}C NMR: δ48.1 (C-1), 68.9 (C-2), 78.3 (C-3), 43.6 (C-4), 48.1 (C-5), 18.5 (C-6), 33.2 (C-7), 40.1 (C-8), 48.0 (C-9), 38.3 (C-10), 23.8 (C-11), 125.6 (C-12), 139.3 (C-13), 42.6 (C-14), 28.7 (C-15), 24.9 (C-16), 48.6 (C-17), 53.6 (C-18), 39.4 (C-19), 39.5 (C-20), 31.1 (C-21), 37.5 (C-22), 66.6 (C-23), 14.4 (C-24), 17.5 (C-25), 17.5 (C-26), 23.9 (C-27), 179.9 (C-28), 17.5 (C-29), 21.4 (C-30).

Scheffoleoside B (**4**). Powder, negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 955.4905 $C_{48}H_{75}O_{19}$ requires 955.4903. $[\alpha]_D^{16}$ −4.8° (pyridine, *c* 0.51), ^{1}H NMR: δ0.90, 0.90, 1.06, 1.08, 1.21, 1.43 (each 3H, *s*), 1.71 (3H, *d*, *J* = 6.2 Hz, Me of Rha), 3.18 (1H, *dd*, *J* = 3.5, 13.4 Hz, H-18), 4.99 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc), 5.40 (1H, *br s*, H-12), 5.85 (1H, *br s*, H-1 of Rha), 6.23 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc), 9.63 (1H, *s*, –CHO); ^{13}C NMR: see Table 1.

Scheffursoside C (**5**). Powder, negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 1073.5539 $C_{53}H_{85}O_{22}$ requires 1073.5533. $[\alpha]_D^{18}$ +2.3° (pyridine; *c* 0.47). ^{1}H NMR: δ0.88 (3H, *d*, *J* = 6.6 Hz), 0.92 (3H, *d*, *J* = 6.4 Hz), 0.94, 1.00, 1.13, 1.17 (each 3H, *s*), 1.71 (3H, *d*, *J* = 6.2 Hz, Me of Rha), 2.50 (1H, *d*, *J* = 11.4 Hz, H-18), 3.70 (1H, *dd*, *J* = 4.7, 11.0 Hz, H-3), 4.97 (1H, *d*, *J* = 6.1 Hz, H-1 of Ara), 4.98 (1H, *d*, *J*

= 8.1 Hz, H-1 of Glc), 5.44 (1H, *br s*, H-12), 5.86 (1H, *br s*, H-1 of Rha), 6.20 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc); ^{13}C NMR: see Table 1.

Cauloside D (**6**). Powder, $[\alpha]_D^{18}$ +7.6° (pyridine, *c* 0.38), ^{1}H NMR: δ0.87, 0.89, 0.94, 0.99, 1.12, 1.18 (each 3H, *s*), 1.68 (3H, *d*, *J* = 6.2 Hz, Me of Rha), 3.18 (1H, *dd*, *J* = 3.5, 13.4 Hz, H-18), 3.70 (1H, *dd*, *J* = 4.7, 11.4 Hz, H-3), 4.98 (1H, *d*, *J* = 6.8 Hz, H-1 of Ara), 4.99 (1H, *d*, *J* = 6.8 Hz, H-1 of Glc), 5.41 (1H, *br s*, H-12), 5.86 (1H, *br s*, H-1 of Rha), 6.24 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc); ^{13}C NMR: see Table 1.

Scheffursoside D (**7**). Powder, $[\alpha]_D^{16}$ −16.4° (MeOH; *c* 0.5). ^{1}H NMR: δ0.86 (3H, *d*, *J* = 6.6 Hz), 0.90 (3H, *d*, *J* = 6.4 Hz), 1.05, 1.07, 1.23, 1.48 (each 3H, *s*), 1.70 (3H, *d*, *J* = 6.2 Hz, Me of Rha), 2.50 (1H, *d*, *J* = 11.2 Hz, H-18), 3.67 (1H, *dd*, *J* = 4.3, 8.8 Hz, H-3), 4.98 (1H, *d*, *J* = 7.9 Hz, H-1 of Glc), 5.46 (1H, *br s*, H-12), 5.85 (1H, *br s*, H-1 of Rha), 6.19 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc); ^{13}C NMR: see Table 1.

Scheffoleoside D (**8**). Powder, $[\alpha]_D^{10}$ −19.4° (pyridine, *c* 1.0), negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 955.4919 $C_{48}H_{75}O_{19}$ requires 955.4903. ^{1}H NMR: δ0.85, 0.88, 1.05, 1.12, 1.19, 1.49 (each 3H, *s*), 1.70 (3H, *d*, *J* = 6.2 Hz, Me of Rha), 3.18 (1H, *dd*, *J* = 4.5, 9.5 Hz, H-18), 4.98 (1H, *d*, *J* = 7.7 Hz, H-1 of Glc), 5.44 (1H, *br s*, H-12), 5.85 (1H, *br s*, H-1 of Rha), 6.23 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc); ^{13}C NMR: see Table 1.

Scheffursoside E (**9**). Powder, negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 1425.6530 $C_{66}H_{105}O_{33}$ requires 1425.6536. $[\alpha]_D^{20}$ −28.4° (50% MeOH; *c* 0.5). ^{1}H NMR (C_5D_5N/D_2O): δ0.91 (3H, *d*, *J* = 6.6 Hz), 0.92 (3H, *d*, *J* = 6.4 Hz), 0.81, 1.00, 1.08, 1.14, 1.24 (each 3H, *s*), 1.63 (3H, *d*, *J* = 5.7 Hz, CH_3 of Rha), 2.40 (1H, *m*, H-18), 5.41 (1H, *br s*, H-12); ^{13}C NMR: see Table 1.

Cleavage of the ester–glycoside linkage of **9**. A soln of **9** (60 mg), anhydrous LiI (60 mg) and 2,6-lutidine (2 ml) in anhydrous MeOH (1 ml) was heated at 150° for 16 hr. The soln was deionized by passing through a column of Amberlite MB-3 and concd to dryness. A suspension of the residue in H_2O was chromatographed on DIAION HP-20 (H_2O, 10% MeOH, MeOH). The eluate with H_2O gave **9s** and with MeOH gave **9p**.

Compound **9s**. Powder, ^{13}C NMR: β-Glc: δ105.2 (C-1), 74.8 (C-2), 78.1 (C-3), 71.4 (C-4), 76.9 (C-5), 69.8 (C-6), 56.9 (Me), α-Glc: 101.0 (C-1), 73.3 (C-2), 75.2 (C-3), 71.6 (C-4), 72.3 (C-5), 68.6 (C-6), 55.2 (Me), inner-Glc: 104.8 and 104.7 (C-1), 75.2 (C-2), 76.3 (C-3), 78.0 (C-4), 76.8 (C-5), 61.1 (C-6), Rha: 102.1 (C-1), 72.3 (C-2), 72.6 (C-3), 73.7 (C-4), 70.1 (C-5), 18.3 (C-6).

Compound **9p**. Powder, negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 955.4912 $C_{48}H_{75}O_{19}$ requires 955.4902. $[\alpha]_D^{13}$ −5.0° (pyridine; *c* 0.6). ^{13}C NMR: δ38.8 (C-1), 26.2 (C-2), 89.4 (C-3), 39.6 (C-4), 55.8 (C-5), 18.5 (C-6), 33.5 (C-7), 39.9 (C-8), 47.9 (C-9), 36.8 (C-10), 23.6 (C-11), 125.7 (C-12), 139.2 (C-13), 42.5 (C-14), 28.7 (C-15), 24.9 (C-16), 48.1 (C-17), 53.6 (C-18), 39.4 (C-19), 39.5 (C-20), 31.1 (C-21), 37.5 (C-22), 28.3 (C-23), 17.5 (C-24), 15.6 (C-25), 17.4 (C-26), 23.9 (C-27), 179.9 (C-28), 17.0 (C-29), 21.4 (C-30), GlcA: 105.1 (C-1), 84.1 (C-2), 77.7 (C-3), 72.3 (C-4), 75.1 (C-5), Gal: 104.4 (C-1), 84.5 (C-2), 76.4 (C-3), 68.9 (C-4), 77.7 (C-5), 62.5 (C-6), Glc: 106.5 (C-1), 76.7 (C-2), 77.8 (C-3), 71.1 (C-4), 79.2 (C-5), 61.4 (C-6).

Acetylation of **9p**. Ac_2O–pyridine treatment of **9p** for 12 hr at room temp. gave acetylated prosapogenin **9p**.

Methylation of acetylated **9p** *with* CH_2N_2. Acetylated **9p** was treated with Et_2O adsorbed CH_2N_2 to give **9pa**.

Compound **9pa**. Powder, $[\alpha]_D^{15}$ +22.7° ($CHCl_3$; *c* 0.3). ^{1}H NMR: δ0.90 (3H, *d*, *J* = 6.4 Hz), 0.98 (3H, *J* = 6.2 Hz), 0.77, 0.78, 0.96, 1.10, 1.10 (each 3H, *s*), 1.98, 2.02, 2.03, 2.07, 2.07, 2.08, 2.08, 2.16, 2.28 (each 3H, *s*, MeCO–), 3.17 (1H, *dd*, *J* = 4.7, 11.6 Hz, H-3α), 3.67, 3.77 (each 3H, *s*, –COOMe), 5.27 (1H, *br s*, H-12), GlcA: 4.65 (1H, *d*, *J* = 7.5 Hz, H-1), 3.82 (1H, *dd*, *J* = 7.5, 10.1 Hz, H-2), 5.26 (1H, *dd*, *J* = 3.5, 10.1 Hz, H-3), 5.12 (1H, *dd*, *J* = 9.7, 9.9 Hz, H-4), 4.20 (1H, *d*, *J* = 9.9 Hz, H-5), Gal: 4.60 (1H, *d*, *J* = 7.5 Hz, H-1), 3.62 (1H, *dd*, *J* = 7.5, 10.1 Hz, H-2), 4.93 (1H, *dd*, *J* = 3.5, 10.1 Hz, H-3), 5.27 (1H, *dd*, *J* = 0.6, 3.5 Hz, H-4), 5.83 (1H, *ddd*, *J* = 0.6, 6.2, 7.1 Hz, H-5), 4.11 (1H, *dd*, *J* = 7.1, 11.2 Hz, H-6a), 4.05 (1H, *dd*, *J* = 6.2, 11.2 Hz, H-6b), Glc: 4.55 (1H, *d*, *J* = 8.1 Hz, H-1), 4.96 (1H, *dd*, *J* = 8.1, 9.7 Hz, H-2), 5.14 (1H, *dd*, *J* = 9.5, 9.7 Hz, H-3), 5.27 (1H, *dd*, *J* = 9.5, 9.7 Hz, H-4), 3.69 (1H, *ddd*, *J* = 2.0, 3.5, 9.7 Hz, H-5), 4.58 (1H, *dd*, *J* = 2.0, 12.5 Hz, H-6a), 4.13 (1H, *dd*, *J* = 3.5, 12.5 Hz, H-6b).

Scheffoleoside E (**10**). Powder, negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 1425.6530 $C_{66}H_{105}O_{33}$ requires 1425.6536. $[\alpha]_D^{20}$ −16.0° (50% MeOH; *c* 0.5), ^{1}H NMR: δ0.81, 0.91, 0.92, 1.04, 1.15, 1.23, 1.29 (each 3H, *s*), 1.66 (3H, *d*, *J* = 6.2 Hz, Me of Rha), 3.14 (1H, *m*, H-18), 5.43 (1H, *br s*, H-12), 6.15 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc); ^{13}C NMR: see Table 1.

Scheffursoside F (**11**). Powder, negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 957.5090 $C_{48}H_{77}O_{19}$ requires 957.5059. $[\alpha]_D^{13}$ −5.88° (pyridine; *c* 0.8). ^{1}H NMR: δ0.91 (3H, *d*, *J* = 8.2 Hz), 0.92 (3H, *d*, *J* = 6.4 Hz), 1.05, 1.14, 1.15, 1.58 (each 3H, *s*), 1.71 (3H, *d*, *J* = 5.7 Hz, Me of Rha), 2.51 (1H, *d*, *J* = 11.9 Hz, H-18), 3.73 (1H, *d*, *J* = 10.6 Hz, H-24a), 4.48 (1H, *d*, *J* = 10.6 Hz, H-24b), 4.99 (1H, *d*, *J* = 7.9 Hz, H-1 of Glc), 5.42 (1H, *br s*, H-12), 5.87 (1H, *br s*, H-1 of Rha), 6.19 (1H, *d*, *J* = 8.1 Hz, H-1 of Glc); ^{13}C NMR: see Table 1.

Scheffoleoside F (**12**). Powder, negative ion HR-FAB-MS: found $[M-H]^-$ *m/z* 957.5090 $C_{48}H_{77}O_{19}$ requires 957.5059. $[\alpha]_D^{13}$ −3.08° (pyridine, *c* 1.07), ^{1}H NMR: δ0.89, 0.89, 1.04, 1.10, 1.21, 1.58 (each 3H, *s*), 1.72 (3H, *d*, *J* = 6.2 Hz, Me of Rha), 3.19 (1H, *dd*, *J* = 4.0, 12.6 Hz, H-18), 3.74 (1H, *d*, *J* = 11.0 Hz, H-3), 3.96 (1H, *ddd*, *J* = 4.4, 9.7, 11.0 Hz, H-2), 4.99 (1H, *d*, *J* = 7.7 Hz, H-1 of Glc), 5.40 (1H, *br s*, H-12), 5.87 (1H, *br s*, H-1 of Rha), 6.24 (1H, *d*, *J* = 8.2 Hz, H-1 of Glc); ^{13}C NMR: see Table 1.

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