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Triterpenoid saponins from the ground part of *Aster ageratoides* var. *ovatus*

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Abstract

Eight new oleanane-type triterpene glycosides, ageratosides A_1–A_5, B_1, B_2 and C_1, were isolated from the ground part of *Aster ageratoides* Turcz. var. *ovatus* Nakai (Compositae) along with scaberoside A_2. Their structures were determined based on spectral and chemical evidence as follows. Ageratoside A_1, 3-*O*-[*O*-β-D-xylopyranosyl-(1→4)-β-D-glucopyranosyl] 2β,3β,16α-trihydroxyolean-12-ene-23,28-dioic acid (zanhic acid) 28-*O*-β-D-apiofuranosyl-(1→3)-*O*-(4-*O*-acetyl)-α-L-rhamnopyranosyl-(1→2)-*O*-α-L-arabinopyranosyl ester; ageratoside A_2, 3-*O*-[*O*-β-D-glucopyranosyl-(1→4)-β-D-glucopyranosyl] zanhic acid 28-*O*-β-D-apiofuranosyl-(1→3)-*O*-(4-*O*-acetyl)-α-L-rhamnopyranosyl-(1→2)-*O*-α-L-arabinopyranosyl ester; ageratoside A_3, 3-*O*-[*O*-β-D-xylopyranosyl-(1→4)-β-D-glucopyranosyl] zanhic acid 28-*O*-α-L-arabinopyranosyl-(1→3)-*O*-(4-*O*-acetyl)-α-L-rhamnopyranosyl-(1→2)-*O*-α-L-arabinopyranosyl ester; ageratoside A_4, 3-*O*-β-D-glucopyranosyl zanhic acid 28-*O*-α-L-arabinopyranosyl-(1→3)-*O*-(4-*O*-acetyl)-α-L-rhamnopyranosyl-(1→2)-*O*-α-L-arabinopyranosyl ester; ageratoside A_5, 3-*O*-β-D-glucopyranosyl zanhic acid 28-*O*-β-D-apiofuranosyl-(1→3)-*O*-(4-*O*-acetyl)-α-L-rhamnopyranosyl-(1→2)-*O*-α-L-arabinopyranosyl ester; ageratoside B_1, 3-*O*-β-D-glucopyranosyl 2β,3β-dihydroxyolean-12-ene-23,28-dioic acid (medicagenic acid) 28-*O*-β-D-glucopyranosyl-(1→6)-*O*-β-D-glucopyranosyl ester; ageratoside B_2, 3-*O*-[*O*-β-D-xylopyranosyl-(1→4)-β-D-glucopyranosyl] medicagenic acid 28-*O*-β-D-xylopyranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→2)-*O*-α-L-arabinopyranosyl ester; and ageratoside C_1, 3-*O*-[*O*-β-D-xylopyranosyl-(1→4)-β-D-glucopyranosyl] 2β,3β,16α,21β-tetrahydroxyolean-12-ene-23,28-dioic acid 21,28-lactone.

Keywords: *Aster ageratoides* var. *ovatus*; Compositae; Saponins; Triterpene glycosides; Ageratosides; Zanhic acid; Medicagenic acid

1. Introduction

In the series of previous papers, we reported the structures of the oleanane-type triterpene glycosides isolated from *Aster tataricus* L. f. (Tanaka, Nagao, Okabe, & Yamauchi, 1990) and *A. scaber* Thunb (Nagao, Iwase, & Okabe, 1993).

Aster ageratoides is used in Chinese traditional medicine for the treatment of fevers, colds, coughs and so on; the antitussive and expectorant activities of the decoction of the herb were described in the "Dictionary of Chinese Crude Drugs" (Chian Su New Medical College, 1977). These descriptions thus suggested the presence of saponins in *Aster ageratoides*. As a continuation of the chemical investigation of the saponin constituents of *Aster* species, *Aster ageratoides* Turcz. var. *ovatus* Nakai, one of the varieties grown in Japan (Ohwi, 1965) was investigated for triterpene glycosides.

2. Results and discussion

From the less polar glycoside fraction, nine compounds (**1**–**9**) were isolated as described in Section 3. The NMR spectra suggested that all of these compounds are glycosides of oleanane-type triterpenes.

By comparison of the physical and spectral data with those of the reported data, the aglycone moiety of **1**–**5** was identified with 2β,3β,16α-trihydroxy-

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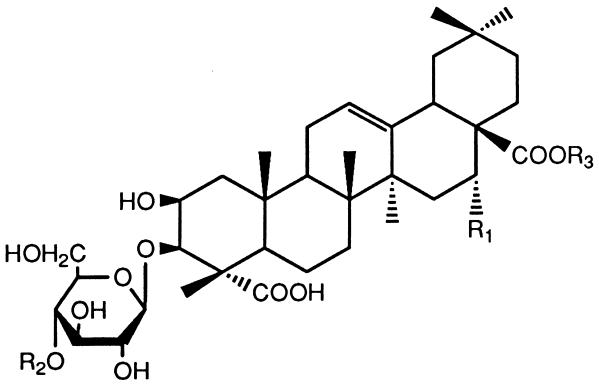
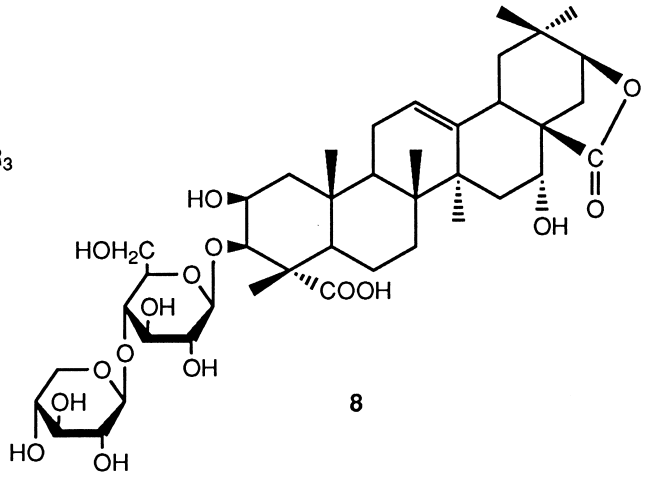


	R_1	R_2	R_3
1	OH	Xyl	Ara^2–Rha^3–Api (4-Ac)
2	OH	Glc	Ara^2–Rha^3–Api (4-Ac)
3	OH	Xyl	Ara^2–Rha^3–Ara (4-Ac)
4	OH	H	Ara^2–Rha^3–Ara (4-Ac)
5	OH	H	Ara^2–Rha^3–Api (4-Ac)
6	H	H	Glc^6–Glc
7	H	Xyl	Ara^2–Rha^3–Xyl
10	OH	Xyl	H



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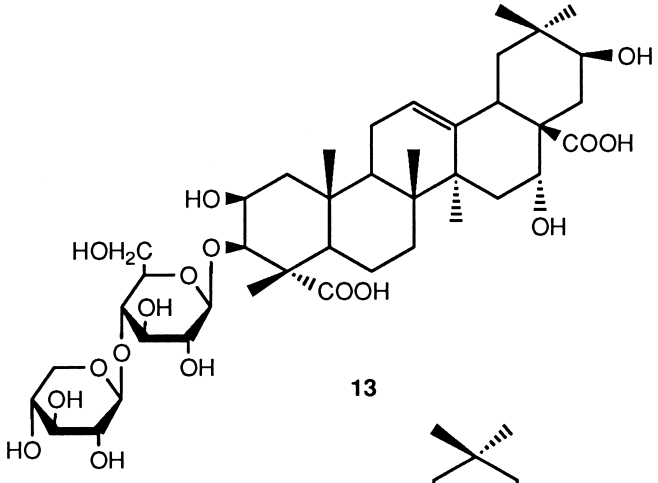

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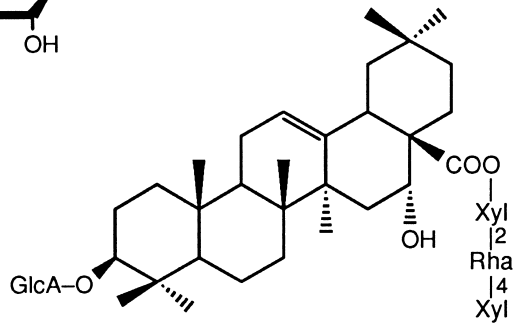

9

olean-12-ene-23,28-dioic acid (zanhic acid) (Oleszekw et al., 1992).

Compound **1** showed an $[M + Na]^+$ ion peak at *m/z* 1287 in the positive ion FABMS, and its high resolution FABMS analysis established the molecular formula, $C_{59}H_{92}O_{29}$. On acid hydrolysis, **1** gave D-apiose (Api), L-arabinose (Ara), D-xylose (Xyl), L-rhamnose (Rha) and D-glucose (Glc) as component sugars. The ^1H NMR spectrum (Table 1) showed the signals of five sugar anomeric protons and protons of one acetyl group, suggesting **1** is a zanhic acid pentaoside monoacetate. In the ^{13}C NMR spectrum (Tables 2 and 3), one anomeric carbon signal appeared at δ 93.5 suggesting the presence of an ester-linked sugar moiety. Compound **1** provided prosapogenin (**10**) and an anomeric mixture (**11**) of a methyl trioside on selective cleavage of the ester sugar linkage (Ohtani, Mizutani, Kasai, & Tanaka, 1984). Prosapogenin **10**, $C_{41}H_{63}O_{16}$, gave D-Xyl and D-Glc on acid hydrolysis and it showed ion peaks at *m/z* 811 ($[M–H]^-$), 679 ($[811\text{-Xyl}]^-$) and 517 ($[679\text{-Glc}]^-$) in the negative ion FABMS, indicating that **10** is a xylosyl-glucoside of zanhic acid. In the HMBC spectrum of **10**, the anomeric carbon signal at δ 105.2 was correlated with a proton signal at δ 4.68 (d, $J = 4$ Hz) which was assigned to H-3 of the aglycone and the other anomeric carbon signal (δ 105.5) was correlated to the proton signal at δ 4.23 (dd, $J = 9$, 9 Hz) which was assigned to H-4 of

Glc. From this spectral evidences, the structure of **10** was established to be 3-*O*-[*O*-β-D-xylopyranosyl-(1→4)-β-D-glucopyranosyl] zanhic acid.

Compound **11** gave D-Api, L-Ara and L-Rha on acid hydrolysis. Its negative ion FABMS showed ion peaks at *m/z* 441 ([M–H]$^-$), 309 ([441-pentosyl group]$^-$) and 163 ([309-Rha]$^-$) showing **11** is a methyl pentosyl–rhamnosyl-pentoside. The α- (**11a**) and β- (**11b**) anomers were separated by prep. HPLC. In the ^{13}C NMR spectrum of **11b**, five characteristic carbon signals (δ 65.6, 74.9, 77.8, 80.8 and 111.7) were observed which were assignable to a terminal apiofuranosyl group. These data suggested that **11** is methyl apiofuranosyl–rhamnopyranosyl-arabinoside. The NMR signals of **11b** were fully assigned as shown in Table 4 by using ^{1}H–^{1}H COSY and ^{1}H-^{13}C COSY techniques. The HMBC spectrum showed C–H correlations between δ 111.7 (C-1 of Api) and δ 4.55 (H-3 of Rha), δ 80.3 (C-3 of Rha) and δ 6.01 (H-1 of Api), δ 104.4 (C-1 of Rha) and δ 4.58 (H-2 of Ara) and δ 78.8 (C-2 of Ara) and δ 5.62 (H-1 of Rha). From these results, the structure of **11b** was determined to be methyl *O*-β-D-apiofuranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→2)-*O*-β-L-arabinopyranoside and **11a** as the α-anomer.

Combining the structures of the prosapogenin (**10**) and the methyl glycoside (**11**), the structure of the desacetyl compound **1** was determined to be 3-*O*-[*O*-β-D-xylopyranosyl-(1→4)-β-D-glucopyranosyl] zanhic acid 28-*O*-β-D-apiofuranosyl-(1→3)-*O*-(4-*O*-acetyl)-α-L-rhamnopyranosyl-(1→2)-*O*-L-arabinopyranosyl ester. The position of the acetyl group in **1** was determined to be C_4-OH of Rha judging from the ^{1}H NMR chemical shift (δ 5.84) of H-4 which appeared at a much lower magnetic field than the corresponding H-4 (δ 4.35) of the rhamnopyranosyl group of **11a**. The configuration and conformation of the ester-linked arabinopyranosyl group of **1** were determined to be α and $^1C_4$ from the coupling constants, J_{H1-H2} (3 Hz) and J_{C1-H1} (171 Hz) (Bock, & Pedersen, 1974). From these results, the structure of **1** was determined as shown. Compound **1** was a new glycoside and named ageratoside A_1.

Compound **2**, named ageratoside A_2, $C_{60}H_{94}O_{30}$, gave D-Api, L-Ara, L-Rha and D-Glc on acid hydrolysis. The NMR spectra of **2** were very similar to those of **1**. The difference is the lack of signals of a xylopyranosyl group and the addition of signals of a glucopyranosyl group. By the ^{1}H–^{1}H COSY, ^{1}H–^{13}C COSY, and HMBC examination, it proved that the xylopyranosyl group in **1** is replaced by a glucopyranosyl group in **2**.

Compound **3**, ageratoside A_3, $C_{59}H_{92}O_{29}$, gave L-Ara, D-Xyl, L-Rha and D-Glc. The NMR spectra were very similar to those of **1**. However, the signals of the terminal apiosyl group of **1** was replaced by the signals of an arabinosyl group. On selective cleavage of the ester sugar linkage, **3** provided a prosapogenin (**10**) and an anomeric mixture (**12**) of a methyl trioside, which is composed of L-Ara and L-Rha. Compound **12** showed the ion peaks at *m/z* 441 ([M-H]$^-$), 309 ([441-Ara]$^-$) and 163 ([309-Rha]$^-$), suggesting **12** to be a methyl arabinosyl–rhamnosyl–arabinoside. The α- (**12a**) and β- (**12b**) anomers were separated by prep. HPLC and their NMR spectroscopic signals were assigned as shown in Table 4. In the HMBC spectrum of **12b**, cross-peaks were observed between δ 106.9 (C-1 of outer Ara) and δ 4.57 (H-3 of Rha), δ 82.9 (C-3 of Rha) and δ 5.01 (H-1 of outer Ara), δ 104.6 (C-1 of Rha) and δ 4.60 (H-2 of Me-Ara) and δ 78.8 (C-2 of Me-Ara) and δ 5.63 (H-1 of Rha). From these results, the structure of **12b** was determined to be methyl *O*-β-D-arabinopyranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→2)-*O*-β-L-arabinopyranoside. Compound **12a** is the α-anomer.

The configuration and conformation of the ester-linked arabinopyranosyl group in **3** were determined to be α and $^1C_4$ by the coupling constants, J_{H1-H2} (3 Hz) and J_{C1-H1} (171 Hz). The structure of **3** was finally determined as shown.

Compound **4**, ageratoside A_4, has the molecular formula $C_{54}H_{84}O_{25}$, $C_5H_8O_4$ (pentosyl group) less than that of **3**. On acid hydrolysis, **4** gave L-Ara, L-Rha and D-Glc. The structure of **4** was determined to be desxylosyl **3** by careful comparison of its NMR data with those of **3**.

Compound **5**, ageratoside A_5, $C_{54}H_{84}O_{25}$, gave L-Ara, L-Rha, D-Api and D-Glc. Its structure was established to be desxylosyl **1** by comparison of its NMR data with those of **1**.

Compounds **6** and **7** proved to be glycosides of 2β,3β-dihydroxyolean-12-ene-23,28-dioic acid (medicagenic acid) by comparison of ^{13}C NMR data of their aglycone moieties with that of asterbatanoside J (Shao et al., 1995).

Compound **6**, ageratoside B_1, $C_{48}H_{76}O_{21}$, gave D-Glc. The NMR spectra showed that **6** is a bisdesmoside having a glucosyl group and a gentiobiosyl group, one at C-3 and the other linked to a carboxyl group by an ester linkage. The HMBC spectrum showed C-H correlations between δ 86.1 (C-3 of the aglycone) and δ 5.09 (H-1 of Glc), δ 176.4 (C-28 of the aglycone) and δ 6.22 (H-1 of the ester-linked inner Glc) and δ 69.4 (C-6 of the ester-linked inner Glc) and δ 5.01 (H-1 of the ester-linked outer Glc). Thus, the structure of **6** was established as shown.

Compound **7**, ageratoside B_2, $C_{57}H_{90}O_{27}$, gave L-Ara, D-Xyl, L-Rha and D-Glc. Its NMR and MS data suggested that **7** has an *O*-β-D-xylopyranosyl-(1→4)-β-D-glucopyranosyl group attached to C_3-OH and a triose composed of L-Ara, L-Rha and D-Xyl linked to C_{17}-COOH group by an ester linkage. The NMR signals were assigned as shown in the tables and the HMBC spectrum showed C–H correlations between δ

Table 1
^{1}H-NMR assignments of **1**–**10** and **13**. The figures following multiplicity (s, d, or dd) in parentheses indicate the coupling constants (J_{H-H}) in Hz

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**13**
Aglycone moiety											
2	ca. 4.76	ca. 4.76	ca. 4.76	ca. 4.82	ca. 4.81	ca. 4.79	4.73 (d-like)	ca. 4.75	ca. 2.25	4.76 (d-like)	ca. 4.76
3	4.68 (d, 4)	4.68 (d, 4)	4.69 (d, 4)	4.73 (d, 3)	4.73 (d, 3)	4.69 (d, 3)	4.65 (d, 3)	4.65 (d, 4)	3.39 (dd, 4, 12)	4.68 (d, 4)	4.68 (d, 4)
12	5.64 (dd, 3, 3)	5.64 (dd, 3, 3)	5.64 (dd, 3, 3)	5.64 (dd, 3, 3)	5.64 (dd, 3, 3)	5.43 (dd, 3, 3)	5.44 (dd, 3, 3)	5.37 (dd, 3, 3)	5.61 (dd, 3, 3)	5.64 (dd, 3, 3)	5.69 (dd, 3, 3)
16	5.18 (br s)	5.18 (br s)	5.18 (br s)	5.18 (br s)	5.18 (br s)	ca. 1.90 (2H)	ca. 1.90 (2H)	4.50 (dd, 5, 11)	5.26 (br s)	5.20 (br s)	5.23 (br s)
23	–	–	–	–	–	–	–	–	1.29 (3H, s)	–	–
24	2.00 (3H, s)	1.98 (3H, s)	1.98 (3H, s)	1.98 (3H, s)	2.00 (3H, s)	1.98 (3H, s)	1.95 (3H, s)	1.97 (3H, s)	0.97 (3H, s)	1.97 (3H, s)	1.97 (3H, s)
25	1.60 (3H, s)	1.59 (3H, s)	1.61 (3H, s)	1.61 (3H, s)	1.61 (3H, s)	1.57 (3H, s)	1.52 (3H, s)	1.50 (3H, s)	0.83 (3H, s)	1.56 (3H, s)	1.57 (3H, s)
26	1.18 (3H, s)	1.17 (3H, s)	1.19 (3H, s)	1.19 (3H, s)	1.18 (3H, s)	1.14 (3H, s)	1.11 (3H, s)	0.85 (3H, s)	1.09 (3H, s)	1.08 (3H, s)	1.08 (3H, s)
27	1.80 (3H, s)	1.80 (3H, s)	1.80 (3H, s)	1.80 (3H, s)	1.81 (3H, s)	1.23 (3H, s)	1.24 (3H, s)	1.33 (3H, s)	1.82 (3H, s)	1.82 (3H, s)	1.84 (3H, s)
29	1.00 (3H, s)	1.00 (3H, s)	1.00 (3H, s)	1.00 (3H, s)	1.00 (3H, s)	0.87 (3H, s)	0.90 (3H, s)	0.93 (3H, s)	0.99 (3H, s)	1.04 (3H, s)	1.34 (3H, s)
30	1.14 (3H, s)	1.13 (3H, s)	1.14 (3H, s)	1.14 (3H, s)	1.14 (3H, s)	0.88 (3H, s)	0.99 (3H, s)	1.06 (3H, s)	1.06 (3H, s)	1.17 (3H, s)	1.42 (3H, s)
C3-O-sugars											
	Glc	**Glc**	**Glc**	**Glc**	**Glc**	**Glc**	**Glc**	**Glc**	**Glc A**	**Glc**	**Glc**
1	5.04 (d, 8)	5.04 (d, 8)	5.05 (d, 8)	5.10 (d, 8)	5.10 (d, 8)	5.09 (d, 8)	5.04 (d, 9)	5.04 (d, 8)	5.00 (d, 8)	5.05 (d, 8)	5.06 (d, 8)
2	3.93 (dd, 8, 9)	3.92 (dd, 8, 9)	3.94 (dd, 8, 9)	3.93 (dd, 8, 9)	3.93 (dd, 8, 9)	3.92 (dd, 8, 8)	3.95 (dd, 9, 9)	3.93 (dd, 8, 9)	4.11 (dd, 8, 8)	3.95 (dd, 8, 9)	3.94 (dd, 8, 9)
3	4.14 (dd, 9, 9)	ca. 4.15	4.15 (dd, 9, 9)	ca. 4.14	ca. 4.14	ca. 4.24	4.15 (dd, 9, 9)	4.14 (dd, 9, 9)	4.30 (dd, 8, 8)	4.13 (dd, 9, 9)	4.16 (dd, 9, 9)
4	4.23 (dd, 9, 9)	4.25 (dd, 9, 9)	4.24 (dd, 9, 9)	ca. 4.14	ca. 4.15	4.31 (dd, 8, 8)	ca. 4.23	4.22 (dd, 9, 9)	4.58 (dd, 8, 9)	4.23 (dd, 9, 9)	4.23 (dd, 9, 9)
5	3.85 (m)	3.86 (m)	3.86 (m)	3.91 (m)	3.92 (m)	ca. 3.86	3.85 (m)	3.85 (m)	4.66 (d, 9)	3.86 (m)	3.86 (m)
6	ca. 4.39	ca. 4.40	ca. 4.42	ca. 4.29	ca. 4.28	ca. 4.30	ca. 4.35	4.40 (dd, 3, 12)	-	4.41 (dd, 3, 12)	4.40 (dd, 3, 12)
	ca. 4.48	ca. 4.47	ca. 4.49	ca. 4.46	ca. 4.46	ca. 4.45	ca. 4.50	4.46 (dd, 4, 12)		4.48 (dd, 4, 12)	4.48 (dd, 4, 12)
	Xyl	**Glc**	**Xyl**				**Xyl**	**Xyl**		**Xyl**	**Xyl**
1	5.05 (d, 8)	5.13 (d, 8)	5.06 (d, 8)				5.05 (d, 8)	5.05 (d, 8)		5.05 (d, 8)	5.05 (d, 8)
2	3.93 (dd, 8, 9)	4.03 (dd, 8, 9)	3.96 (dd, 8, 9)				3.96 (dd, 8, 8)	3.95 (dd, 8, 9)		3.97 (dd, 8, 9)	3.96 (dd, 8, 9)
3	4.06 (dd, 9, 9)	ca. 4.17	4.06 (dd, 9, 9)				4.07 (dd, 8, 8)	4.05 (dd, 9, 9)		4.07 (dd, 9, 9)	4.06 (dd, 9, 9)
4	4.11 (m)	ca. 4.13	ca. 4.12				ca. 4.15	ca. 4.10		4.11 (m)	ca. 4.11
5	3.63 (d-like)	ca. 3.94	3.62 (dd, 10, 11)				ca. 3.62	3.62 (dd, 10, 11)		ca. 3.62	3.62 (dd, 10, 11)
	ca. 4.21		ca. 4.21				ca. 4.21	4.20 (dd, 5, 11)		4.20 (dd, 5, 11)	4.20 (dd, 5, 11)
6	–	ca. 4.23 and 4.45	–				–	–		–	–

Table 1 (*continued*)

	1	2	3	4	5	6	7	8	9	10	13
C17-COO-sugars											
	Ara	**Ara**	**Ara**	**Ara**	**Ara**	**Glc**	**Ara**		**Xyl**		
1	6.43 (d, 3)	6.42 (d, 3)	6.44 (d, 3)	6.42 (d, 3)	6.43 (d, 3)	6.22 (d, 8)	6.48 (d, 3)		6.13 (d, 7)		
2	4.52 (dd, 3, 4)	4.52 (dd, 3, 4)	4.54 (dd, 3, 4)	4.54 (dd, 3, 4)	4.43 (dd, 3, 4)	4.10 (dd, 8, 9)	4.53 (dd, 3, 4)		4.32 (dd, 7, 7)		
3	ca. 4.48	ca. 4.45	ca. 4.47	ca. 4.42	ca. 4.48	4.19 (dd, 9, 9)	ca. 4.50		ca. 4.21		
4	ca. 4.41	ca. 4.40	ca. 4.38	4.38 (m)	ca. 4.40	ca. 4.29	ca. 4.40		ca. 4.15		
5	ca. 3.92	ca. 3.94	ca. 3.90	ca. 3.88	ca. 3.94	ca. 4.10	ca. 3.93		3.78 (dd, 9, 11)		
	ca. 4.48	ca. 4.50	ca. 4.49	ca. 4.47	ca. 4.48		ca. 4.47		ca. 4.33		
6	–	–	–	–	–	ca. 4.35 and 4.69	–		–		
	Rha	**Rha**	**Rha**	**Rha**	**Rha**	**Glc**	**Rha**		**Rha**		
1	5.78 (br s)	5.78 (br s)	5.78 (br s)	5.80 (br s)	5.80 (br s)	5.01 (d, 8)	5.71 (br s)		6.34 (br s)		
2	4.76 (br s)	4.76 (br s)	4.82 (br s)	4.82 (br s)	4.76 (br s)	3.97 (dd, 8, 9)	ca. 4.55		4.74 (br s)		
3	ca. 4.48	ca. 4.46	4.53 (dd, 3, 10)	4.56 (dd, 3, 10)	ca. 4.48	ca. 4.20	ca. 4.35		4.67 (dd, 3, 9)		
4	5.84 (dd, 10, 10)	5.83 (dd, 10, 10)	5.86 (dd, 10, 10)	5.86 (dd, 10, 10)	5.85 (dd, 10, 10)	ca. 4.15	ca. 4.55		4.41 (dd, 9, 9)		
5	ca. 4.43	ca. 4.40	ca. 4.45	ca. 4.41	ca. 4.43	ca. 3.86	ca. 4.37		4.49 (dq, 6, 9)		
6	1.38 (3H, d, 6)	1.38 (3H, d, 6)	1.42 (3H, d, 6)	1.42 (3H, d, 6)	1.38 (3H, d, 6)	ca. 4.30 and 4.45	1.77 (3H, d, 6)		1.76 (3H, d, 6)		
OAc	2.14 (3H, s)	2.15 (3H, s)	2.24 (3H, s)	2.24 (3H, s)	2.14 (3H, s)	–	–		–		
	Api	**Api**	**Ara**	**Ara**	**Api**		**Xyl**		**Xyl**		
1	5.71 (d, 4)	5.70 (d, 4)	4.86 (d, 7)	4.87 (d, 8)	5.71 (d, 3)		5.10 (d, 7)		5.19 (d, 7)		
2	4.53 (d, 4)	4.54 (d, 4)	ca. 4.26	ca. 4.27	4.54 (d, 3)		ca. 4.00		ca. 4.05		
3	–	–	ca. 4.07	4.10 (dd, 3, 9)	–		ca. 4.05		ca. 4.07		
4	4.21 (d, 9)	4.26 (d, 9)	ca. 4.21	ca. 4.24	4.21 (d, 9)		ca. 3.65		ca. 4.10		
	4.47 (d, 9)	4.48 (d, 9)			4.47 (d, 9)						
5	ca. 3.95 (2H)	ca. 3.97 (2H)	3.67 (d-like)	3.68 (d-like)	ca. 3.95 (2H)		3.50 (dd, 10, 11)		3.48 (dd, 9, 11)		
			ca. 4.13	ca. 4.12			ca. 4.23		ca. 4.21		

Table 2
^{13}C-NMR spectral assignments for the aglycone moieties of **1**–**10** and **13**

	1	2	3	4	5	6	7	8	9	10	13
1	44.2	44.4	44.3	44.3	44.3	44.2	44.2	44.0	38.8	44.2	44.3
2	70.1	70.3	70.2	70.2	70.1	70.2	70.2	70.1	26.6	70.2	70.3
3	86.2	86.1	86.1	86.0	86.0	86.1	86.2	86.1	89.1	86.2	86.3
4	52.8	52.9	52.8	52.9	52.8	52.8	52.8	52.8	39.5	52.8	52.9
5	52.6	52.7	52.6	52.5	52.5	52.3	52.4	52.6	55.9	52.5	52.5
6	21.2	21.2	21.3	21.3	21.2	21.2	21.1	21.0	18.7	21.1	21.2
7	33.4	33.5	33.4	33.4	33.4	32.9	33.0	32.4	33.5	33.3	33.4
8	40.5	40.6	40.5	40.5	40.5	40.3	40.3	40.8	40.0	40.3	40.4
9	47.9	47.9	47.8	47.8	47.8	48.7	48.7	48.0	47.1	47.9	47.9
10	36.9	36.9	36.9	36.9	36.9	36.8	36.8	36.8	37.0	36.9	36.9
11	24.0	24.1	24.0	24.0	24.0	23.9	24.0	23.9	23.8	24.0	24.1
12	122.8	122.8	122.8	122.8	122.8	122.8	122.9	124.4	122.5	122.3	122.6
13	144.4	144.5	144.4	144.4	144.3	144.1	144.2	140.2	144.4	145.1	144.5
14	42.2	42.3	42.2	42.2	42.2	42.2	42.2	43.4	42.2	42.2	42.2
15	36.2	36.3	36.2	36.2	36.2	28.2	28.2	38.0	36.3	36.0	35.8
16	73.8	73.9	73.9	73.9	73.7	23.3	23.2	66.6	74.0	74.6	74.3
17	49.5	49.6	49.5	49.5	49.5	47.0	47.3	49.9	49.5	48.8	51.7
18	41.2	41.3	41.2	41.2	41.2	41.7	41.7	41.7	41.5	41.4	41.0
19	47.0	47.1	47.0	47.0	47.0	46.1	46.2	42.8	47.4	47.2	48.5
20	30.9	30.9	30.9	30.9	30.8	30.7	30.9	34.1	30.8	31.0	36.7
21	35.9	36.0	35.9	35.9	35.9	33.9	34.1	83.4	36.1	36.2	73.5
22	32.0	32.1	32.0	32.1	32.0	32.5	32.7	27.2	32.0	32.8	41.8
23	180.4	180.9	180.5	180.9	180.7	180.8	180.6	180.4	28.2	180.5	180.7
24	14.1	14.2	14.2	14.3	14.2	14.2	14.2	14.1	17.0	14.1	14.2
25	17.0	17.0	17.0	17.0	17.0	16.9	16.8	16.9	15.6	16.9	16.9
26	17.5	17.5	17.5	17.5	17.4	17.4	17.4	16.2	17.4	17.4	17.4
27	27.2	27.2	27.2	27.2	27.2	26.1	26.1	28.7	27.1	27.2	27.2
28	175.9	176.0	175.9	175.9	175.9	176.4	176.2	181.1	175.9	179.9	179.2
29	33.2	33.2	33.2	33.2	33.1	33.0	33.1	28.5	33.1	33.3	30.0
30	24.7	24.8	24.7	24.8	24.7	23.6	23.7	24.3	24.5	24.7	18.3

176.2 (C-28 of the aglycone) and δ 6.48 (H-1 of Ara), δ 75.3 (C-2 of Ara) and δ 5.71 (H-1 of Rha), and δ 84.1 (C-3 of Rha) and δ 5.10 (H-1 of the ester-linked terminal Xyl). Thus, the structure of **7** was determined as shown.

Compound **8**, ageratoside C_1, $C_{41}H_{62}O_{16}$, gave D-Xyl and D-Glc. In the negative ion FABMS, **8** showed the ion peaks at m/z 809 ($[M–H]^-$), 677 ($[809\text{-Xyl}]^-$), 515 ($[677\text{-Glc}\ (=\text{aglycone–H})]^-$), indicating **8** is a xylosylglucoside of the aglycone. The NMR spectra suggested **8** is a monodesmosyl bioside of an olean-12-ene type triterpene which has three hydroxyl groups, one carboxyl group and one lactonic group. By comparison of the ^{13}C NMR data of **8** with those of **1**, it proved that the signals of rings A and B and the sugar moiety were superimposable on those of **1**. The ^{13}C NMR data of rings C, D and E moiety of **8**, having one hydroxyl group and one lactonic group, showed good agreement with those of 3β,16α,21β-trihydroxyolean-12-ene-23,28-dioic acid (acacic acid) 28,21-lactone glycoside (Kinjo et al., 1992). The configuration of C_{16}-OH group of **8** was determined to be α because the ^{1}H NMR spectrum of the alkaline hydrolysate (**13**) of **8** showed the signal of H-16 at δ 5.23 as a broad singlet. Therefore, the structure of **8** was determined as shown.

Compound **9** was identified with scaberoside A_2 by direct comparison with authentic sample which was isolated from the root of *Aster scaber* Thunb. (Nagao, Tanaka, Shimokawa, & Okabe, 1991).

3. Experimental

3.1. General

NMR spectra were measured on a JEOL JNM-A500 spectrometer in C_5D_5N using TMS as an internal standard. MS were recorded on a JEOL JMS-HX110 spectrometer by the direct inlet method with glycerol matrix. GC was carried out using a DB-1 column (0.25 mm i.d. × 30 m long, J&W Scientific) with FID. For prep. HPLC, Cosmosil 5C18-AR column (20 mm i.d. × 250 mm in length, Nacalai tesque) was used. For column chromatography, silica gel 60 (63–200 μm, Merck), YMC-Gel ODS-A 120-230/70 (63–200 μm, YMC) and Diaion HP-20 (Mitsubishi Chemical Industry Co.) were used.

Table 3
^{13}C-NMR spectral assignments for the sugar moieties of **1**–**10** and **13**

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**13**
C3-O-sugars											
	Glc	**Glc**	**Glc**	**Glc**	**Glc**	**Glc**	**Glc**	**Glc**	**Glc A**	**Glc**	**Glc**
1	105.1	105.0	105.1	105.2	105.1	105.3	105.1	105.2	107.1	105.2	105.2
2	74.6	74.7	74.8	75.2	75.0	75.1	74.8	74.7	75.5	74.8	74.8
3	76.1	76.5	76.2	78.2	78.1	78.3	76.2	76.1	78.1	76.2	76.2
4	80.7	80.8	80.7	71.5	71.4	71.0	80.7	80.8	73.4	80.8	80.8
5	76.4	76.4	76.4	78.3	78.2	78.3	76.4	76.4	77.7	76.4	76.4
6	61.6	61.9	61.7	62.6	62.5	62.7[a]	61.7	61.7	172.8	61.7	61.7
	Xyl	**Glc**	**Xyl**				**Xyl**	**Xyl**		**Xyl**	**Xyl**
1	105.4	104.8	105.5				105.4	105.4		105.5	105.4
2	74.7	74.7	74.8				74.8	74.8		74.8	74.8
3	78.1	78.2	78.2				78.2	78.2		78.2	78.2
4	70.6	71.5	70.7				70.9	70.7		70.7	70.7
5	67.3	78.4	67.3				67.3	67.3		67.3	67.3
6	–	62.4	–				–	–		–	–
C17-COO-sugar											
	Ara	**Ara**	**Ara**	**Ara**	**Ara**	**Glc**	**Ara**		**Xyl**		
1	93.5	93.6	93.6	93.6	93.5	95.6	93.4		95.2		
2	75.8	75.8	75.4	75.4	75.7	73.8	75.3		75.7		
3	70.5	70.6	70.2	70.4	70.5	78.3	69.7		77.7		
4	66.2	66.4	66.2	66.3	66.2	71.5	65.9		70.8		
5	63.4	63.5	63.4	63.5	63.5	77.9	62.8		67.2		
6	–	–	–	–	–	69.4	–		–		
	Rha	**Rha**	**Rha**	**Rha**	**Rha**	**Glc**	**Rha**		**Rha**		
1	101.4	101.5	101.4	101.4	101.4	105.2	101.0		101.2		
2	71.6	71.7	71.9	71.9	71.5	75.1	71.9		71.9		
3	78.5	78.5	79.1	79.1	78.5	78.7	84.1		72.5		
4	73.5	73.6	73.5	73.5	73.5	71.5	72.6		83.6		
5	67.9	67.9	68.0	68.0	67.8	78.3	68.6		68.4		
6	17.9	17.9	17.9	17.9	17.9	62.6[a]	18.3		18.6		
OAc	20.9	21.0	21.2	21.3	20.9	–	–		–		
	170.4	170.6	170.6	170.7	170.4	–	–		–		
	Api	**Api**	**Ara**	**Ara**	**Api**		**Xyl**		**Xyl**		
1	112.2	112.2	107.1	107.1	112.1		107.1		106.7		
2	77.6	77.8	71.9	71.9	77.6		76.0		76.0		
3	79.5	79.7	74.4	74.3	79.5		78.5		78.6		
4	74.8	74.9	69.5	69.4	74.8		70.7		71.0		
5	65.0	65.1	67.1	67.0	65.0		67.4		67.4		

[a] These assignments may be interchanged.

3.2. Plant material

Aster ageratoides was first commercially obtained and then cultivated at the medicinal plant garden of Fukuoka University. A voucher specimen was deposited in the Herbarium of Faculty of Pharmaceutical Sciences, Fukuoka University.

3.3. Extraction and isolation

The dried and powdered ground part (2 kg) was percolated with $CHCl_3$ and then with 50% MeOH. The 50% MeOH solution was applied to a Diaion HP-20 column. After washing the column with 50% MeOH, the crude glycoside fraction was eluted with MeOH.

Table 4
^{1}H- and ^{13}C-NMR spectral assignments for the methyl oligoglycosides prepared from **1** and **3**. The figures following multiplicity (s, d, or dd) in parentheses indicate the coupling constants (J_{H-H}) in Hz

	11a		**11b**		**12a**		**12b**	
	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H
-OMe	55.9	3.49 (3H, s)	55.0	3.38 (3H, s)	55.9	3.54 (3H, s)	55.0	3.43 (3H, s)
Ara-1	103.7	4.52 (d, 7)	101.2	5.30 (d, 3)	103.7	4.54 (d, 7)	101.2	5.33 (d, 3)
2	76.9	4.47 (dd, 7, 7)	78.8	4.58 (dd, 3, 9)	76.7	4.50 (dd, 7, 8)	78.8	4.60 (dd, 3, 9)
3	74.2	ca. 4.15	68.9	ca. 4.49	74.3	ca. 4.15	69.0	4.50 (dd, 3, 9)
4	69.3	ca. 4.17	70.8	ca. 4.28	69.3	ca. 4.19	70.7	4.29 (m)
5	66.1	3.66(d-like) ca. 4.20	63.5	3.95 (2H, d-like)	66.1	ca. 3.66 ca. 4.20	63.5	3.96 (2H, d-like)
Rha-1	102.3	5.96 (d, 2)	104.4	5.62 (d, 2)	102.4	6.00 (d, 2)	104.6	5.63 (d, 2)
2	71.9	4.86 (dd, 2, 3)	71.6	4.82 (dd, 2, 3)	71.9	4.92 (dd, 2, 3)	71.5	4.87 (dd, 2, 3)
3	80.4	4.59 (dd, 3, 9)	80.3	4.55 (dd, 3, 9)	83.1	4.62 (dd, 3.9)	82.9	4.57 (dd, 3, 9)
4	72.6	4.35 (dd, 9, 9)	72.5	4.30 (dd, 9, 9)	73.0	4.41 (dd, 9, 9)	72.9	4.36 (dd, 9, 9)
5	69.8	4.62 (dq, 6, 9)	70.0	4.42 (dq, 6, 9)	69.6	4.65 (dq, 6, 9)	69.7	4.46 (dq, 6, 9)
6	18.3	1.60 (3H, d, 6)	18.5	1.58 (d, 6)	18.3	1.58 (3H, d, 6)	18.4	1.56 (3H, d, 6)
	Api				**Ara**			
1	111.9	6.16 (d, 3)	111.7	6.01 (d, 3)	107.1	5.21 (d, 7)	106.9	5.01 (d, 7)
2	77.9	4.75 (d, 3)	77.8	4.69 (d, 3)	73.1	ca. 4.50	73.1	ca. 4.45
3	80.1	–	80.8	–	74.4	4.10 (dd, 3, 9)	74.4	4.04 (dd, 3, 9)
4	75.0	4.26 (d, 9) 4.58 (d, 9)	74.9	4.16 (d, 9) 4.47 (d, 9)	69.3	ca. 4.23	69.3	ca. 4.20
5	65.6	ca. 4.14 (2H)	65.6	4.09 (2H, d-like)	66.9	3.60 (dd, 2, 11) ca. 4.20	66.9	3.45 (dd, 2, 11) 4.11 (dd, 3, 11)

The crude glycoside fraction was applied onto a YMC-Gel ODS column, eluted with 50–70% MeOH, affording two saponin fractions, fr. 1 (polar saponin fraction, 14 g) and fr. 2 (less polar saponin fraction, 13 g). The latter was repeatedly chromatographed on silica gel (EtOAc–MeOH–H_2O; 8:2:1 → 6:2:1) and prep. HPLC (30–35% MeCN and/or 60–70% MeOH) to give nine saponins, **1** (1.01 g), **2** (64 mg), **3** (822 mg), **4** (31 mg), **5** (25 mg), **6** (73 mg), **7** (37 mg), **8** (95 mg) and **9** (170 mg).

3.4. Ageratoside A_1 (*1*)

White powder, $[\alpha]_D^{22}$ −42.8° (MeOH; *c* 1.0). Positive ion FABMS *m/z*: 1287.5605 $[M + Na]^+$, $C_{59}H_{92}NaO_{29}$ requires 1287.5621. Negative ion FABMS *m/z*: 1263 $[M–H]^-$. ^{1}H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3. The coupling constant between C-1 and H-1 ($J_{C1–H1}$) of ester linked Ara, 171 Hz.

3.5. Ageratoside A_2 (*2*)

White powder, $[\alpha]_D^{22}$ −38.9° (MeOH; *c* 1.0). Positive ion FABMS *m/z*: 1317.5719 $[M + Na]^+$, $C_{60}H_{94}NaO_{30}$ requires 1317.5727. Negative ion FABMS *m/z*: 1293 $[M–H]^-$. ^{1}H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3. The coupling constant between C-1 and H-1 ($J_{C1–H1}$) of ester linked Ara, 171 Hz.

3.6. Ageratoside A_3 (*3*)

White powder, $[\alpha]_D^{22}$ −25.7° (MeOH; *c* 1.0). Positive ion FABMS *m/z*: 1287.5615 $[M + Na]^+$, $C_{59}H_{92}NaO_{29}$ requires 1287.5621. Negative ion FABMS *m/z*: 1263 $[M–H]^-$. ^{1}H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3. The coupling constant between C-1 and H-1 ($J_{C1–H1}$) of ester linked Ara, 171 Hz.

3.7. Ageratoside A_4 (*4*)

White powder, $[\alpha]_D^{22}$ −16.7° (MeOH; *c* 1.0). Positive ion FABMS *m/z*: 1155.5197 $[M + Na]^+$, $C_{54}H_{84}NaO_{25}$ requires 1155.5199. Negative ion FABMS *m/z*: 1131 $[M–H]^-$. ^{1}H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3. The coupling constant between C-1 and H-1 ($J_{C1–H1}$) of ester linked Ara, 171 Hz.

3.8. Ageratoside A_5 (*5*)

White powder, $[\alpha]_D^{22}$ −30.9° (MeOH; *c* 0.5). Positive ion FABMS *m/z*: 1155.5210 $[M + Na]^+$, $C_{54}H_{84}NaO_{25}$ requires 1155.5199. Negative ion FABMS *m/z*: 1131 $[M–H]^-$. ^{1}H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3. The coupling constant between C-1 and H-1 ($J_{C1–H1}$) of ester linked Ara, 170 Hz.

3.9. Ageratoside B_1 (**6**)

White powder, $[\alpha]_D^{22}$ +18.3° (MeOH; *c* 0.5). Positive ion FABMS *m/z*: 1011.4777 $[M + Na]^+$, $C_{48}H_{76}NaO_{21}$ requires 1011.4776. Negative ion FABMS *m/z*: 987 $[M–H]^-$. ^1H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3.

3.10. Ageratoside B_2 (**7**)

White powder, $[\alpha]_D^{22}$ −12.8° (MeOH; *c* 0.5). Positive ion FABMS *m/z*: 1229.5562 $[M + Na]^+$, $C_{57}H_{90}NaO_{27}$ requires 1229.5567. Negative ion FABMS *m/z*: 1205 $[M–H]^-$. ^1H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3. The coupling constant between C-1 and H-1 ($J_{C1–H1}$) of ester linked Ara, 174 Hz.

3.11. Ageratoside C_1 (**8**)

White powder, $[\alpha]_D^{22}$ −2.3° (MeOH; *c* 1.0). Positive ion FABMS *m/z*: 833.3957 $[M + Na]^+$, $C_{41}H_{62}NaO_{16}$ requires 833.3935. Negative ion FABMS *m/z*: 809 $[M–H]^-$, 677 $[809\text{-Xyl}]^-$, 515 $[677\text{-Glc}]^-$. ^1H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3.

3.12. Scaberoside A_2 (**9**)

White powder, $[\alpha]_D^{22}$ −41.6° (MeOH; *c* 1.0). Positive ion FABMS *m/z*: 1081.5175 $[M + Na]^+$, $C_{52}H_{82}NaO_{22}$ requires 1081.5195. Negative ion FABMS *m/z*: 1057 $[M–H]^-$. ^1H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3.

3.13. Determination of sugar species and their absolute configurations: general method

3.13.1. Sugar identification

A glycoside (2–3 mg) was dissolved in 1 N HCl–MeOH (1 ml) and heated at 95°C for 2 h. The acidic solution was neutralized with Ag_2CO_3 and the precipitate was removed by centrifugation. The supernatant was concentrated and the residue was trimethylsilylated with TMSi-imidazole and checked by GC. The GC conditions were as follows: column oven temp., 170°C; injection port and detector temp., 250°C; carrier gas, He (linear velocity, 30 cm/s; split ratio, 1/40).

3.13.2. Configuration determination

Determination of the absolute configuration was performed according to the method reported by Hara, Okabe, and Mihashi (1987). A glycoside (5–10 mg) was dissolved in 1 N HCl containing 50% dioxane (1 ml) and heated at 95°C for 2 h. The acidic solution was neutralized in the same manner as described above. The hydrolysate was suspended in H_2O and extracted with $CHCl_3$ to remove the aglycone. The aqueous layer was concentrated and the residue was dissolved in pyridine (0.2 ml). After addition of a pyridine solution (0.4 ml) of L-cysteine methyl ester hydrochloride (0.06 mol/l), the mixture was warmed at 60°C for 1 h. The solvent was removed under an N_2 stream and the residue was checked by GC after trimethylsilylation. The identification was performed by comparison of the retention time with that of the authentic sugar sample. The hydrolysate of apiin was used as a standard for D-apiose. The GC conditions for the determination of the absolute configurations of the component monosaccharides were as follows: column oven temp., 250°C; injection port and detector temp., 290°C; carrier gas, He (linear velocity, 30 cm/s; split ratio, 1/40).

3.14. Selective cleavage of ester glycoside linkages

Selective cleavage of the ester-linked sugar moiety was performed according to the method reported by Ohtani et al. (1984) Compound **1** (500 mg) and dry LiI (1 g) were dissolved in a mixture of dry MeOH (2.5 ml) and 2,6-lutidine (5 ml). The solution was heated at 180°C for 4 h in a sealed tube, then diluted with 50% MeOH and passed through an Amberlite MB-3 column. The eluate was concentrated to dryness and the residue was dissolved in 50% MeOH. The solution was applied on Diaion HP-20 column and the column was eluted with 50% MeOH to give an anomeric mixture of methyl glycosides (**11**, 85 mg) and then, washed with MeOH to give prosapogenin (**10**, 103 mg).

3.15. Prosapogenin (**10**)

White powder, $[\alpha]_D^{22}$ +7.2° (MeOH; *c* 0.5). Negative ion FABMS *m/z*: 811.4120 $[M–H]^-$, $C_{41}H_{63}O_{16}$ requires 811.4116, 679 $[811\text{-Xyl}]^-$, 517 $[679\text{-Glc}]^-$. ^1H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3.

3.16. Anomeric mixture of methyl glycosides (**11**)

White powder. Positive ion FABMS *m/z*: 465 $[M + Na]^+$. Negative ion FABMS *m/z*: 441 $[M–H]^-$, 309 $[441\text{-Api}]^-$, 163 $[309\text{-Rha}]^-$. This anomeric mixture was subjected to prep. HPLC (10% MeOH, as eluant) to give the α-anomer (**11a**, 25 mg) and the β-anomer (**11b**, 35 mg).

11a: white powder, $[\alpha]_D^{20}$ +38.4° (MeOH; *c* 0.9). ^1H and ^{13}C NMR: see Table 4.
11b: white powder, $[\alpha]_D^{20}$ +5.2° (MeOH; *c* 1.8). ^1H and ^{13}C NMR: see Table 4.

Compound **3** (470 mg) was treated in the same way as described for **1** to give prosapogenin (**10**, 98 mg)

and an anomeric mixture (**12**, 120 mg). The latter was separated into the α-anomer (**12a**, 62 mg) and the β-anomer (**12b**, 39 mg).

12: white powder. Positive ion FABMS *m/z*: 465 $[M + Na]^+$. Negative ion FABMS *m/z*: 441 $[M–H]^-$, 309 [441-Ara]$^-$, 163 [309-Rha]$^-$.
12a: white powder, $[\alpha]_D^{20}$ −29.9° (MeOH; *c* 1.3). ^1H and ^{13}C NMR: see Table 4.
12b: white powder, $[\alpha]_D^{20}$ +35.9° (MeOH; *c* 1.8). ^1H and ^{13}C NMR: see Table 4.

3.17. Hydrolysis of **8**

Compound **8** (38 mg) was dissolved in 3% KOH containing 90% MeOH (2 ml) and the solution was stirred at 60°C for 1 h. After neutralization with 15% AcOH, the solution was applied on the Diaion HP-20 column. The column was washed with 50% MeOH and then with MeOH. MeOH eluted hydrolysate **13** (37 mg).

13: white powder, $[\alpha]_D^{19}$ +12.3° (MeOH; *c* 1.0). Positive ion FABMS *m/z*: 851.4043 $[M + Na]^+$, $C_{41}H_{64}NaO_{17}$ requires 851.1041. Negative ion FABMS *m/z*: 827 $[M–H]^-$. ^1H NMR: see Table 1. ^{13}C NMR: see Tables 2 and 3.

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