Pergamon

Tetrahedron Letters 42 (2001) 2825–2828

TETRAHEDRON LETTERS

A novel 3,4-*seco*-migrated-lupane glycoside with a seven-membered B-ring from *Acanthopanax divaricatus* var. *sachunensis*

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Received 19 January 2001; accepted 16 February 2001

Abstract—Sachunoside, a 3,4-*seco*-migrated-lupane glycoside involving a seven-membered B-ring and seven related 3,4-*seco*-lupane tripenoids were isolated from *Acanthopanax divaricatus* Seemann var. *Sachunensis* Yook and their structures were established by a variety of NMR techniques, including ^{1}H–^{1}H COSY and ^{1}H–^{13}C COSY (HMBC, HMBC) methods, and FABMS.

The *Acanthopanax* genus belonging to the Araliaceae family is widely used as a traditional oriental medicine having tonic and prophylactic functions. During the course of our studies on the phytochemical constituents of *Acanthopanax* species,[1–7] sachunoside (**1**, see Fig. 1), a novel 3,4-*seco*-migrated-lupane glycoside and seven related 3,4-*seco*-lupane triterpenoids were isolated from the leaves of *Acanthopanax divaricatus* Seemann var. *Sachunensis* Yook, which was recently found as a new *Acanthopanax* species at Sachun City, Korea. This paper describes the structure elucidation of sachunoside (**1**) and seven 3,4-*seco*-lupane triterpenoids (**2**–**8**).

Sachunoside (**1**), white powder (0.104% yield from the MeOH extract) showing $[\alpha]_D$ −49.0 (MeOH),[8] was obtained by repeated column chromatography on Diaion-HP 20, Sepadex LH-20, silica gel and reverse phase ODS.

The molecular formula $C_{54}H_{84}O_{23}$ of **1** was established by a quasimolecular ion peak $[M+Na]^+$ at m/z 1123 in the positive FABMS and analysis of its ^{13}C NMR spectra (Table 1). The ^{1}H NMR spectrum (in pyridine-d_5) displayed the signals of four tertiary methyl groups, one secondary methyl group, three sets of exomethylene protons, and four anomeric protons [δ 4.93 (d, $J=7.9$ Hz), 5.83 (br s), 6.31 (d, $J=7.9$ Hz), 6.33 (d, $J=7.9$ Hz)]. The ^{13}C NMR spectrum showed 54 signals, of which 30 were originated from the triterpene moiety and 24 from four sugar moieties containing four anomeric carbons (δ 95.3, 96.0, 102.7, 105.1). These data indicated that **1** was a triterpene glycoside, the sugar chain of which was composed of three β-D-glucopyranosyl and one α-L-rhamnopyranosyl moieties.[9] Alkaline hydrolysis of **1** gave two novel sapogenols, named sachunogenin (**1a**), white powder, $[\alpha]_D$ −63.5 (MeOH),[10] and sachunogenin 3-*O*-methyl ester (**1b**), white powder, $[\alpha]_D$ −79.6 (MeOH). Incubation of **1** with esterase, which was prepared from the leaves of *Acanthopanax* species by gel filtration, afforded sachunogenin 3-*O*-glucoside (**1c**), white powder, $[\alpha]_D$ −33.7 (MeOH),[11] as a partially digested product along with **1a**. The EIMS of **1a** showed a quasimolecular ion peak $[M-COOH-H]^+$ at m/z 422. Its molecular formula was assigned as $C_{30}H_{44}O_4$ from the ^{13}C NMR data (Table 1). On the other hand, the EIMS of sachunogenin 3-*O*-methyl ester (**1b**) showed a molecular ion peak at m/z 482 ($[M]^+$, $C_{31}H_{46}O_4$) and a quasimolecular ion peak at m/z 422 ($[M-COOCH_3-H]^+$). Compound **1c** had a molecular formula of $C_{36}H_{54}O_9$ as determined by positive FABMS (m/z 653, $[M+Na]^+$) and ^{13}C NMR spectrum (Table 1). The ^{13}C NMR spectrum of **1a** revealed the presence of 30 carbon atoms, composed of two carboxyl groups, three disubstituted double bonds, six methine carbons, nine methylene carbons, four methyl carbons and three quaternary carbons (Table 1). From the HMBC spectrum of **1a**, one set of exomethylene olefinic protons

Keywords: *Acanthopanax divaricatus* var. *Sachunensis*; Araliaceae; 3,4-*seco*-migrated-lupane; 3,4-*seco*-lupane; sachunoside; triterpene glycoside.

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0040-4039/01/$ - see front matter
PII: S0040-4039(01)00287-8

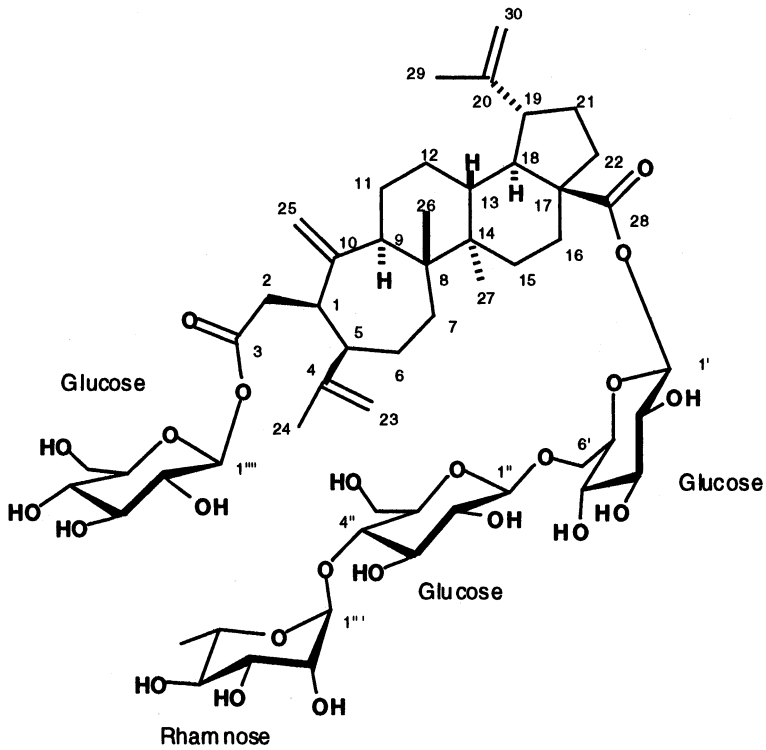

Figure 1. Structure of sachunoside (**1**).

Table 1. ^{13}C NMR data for compounds **1**, **1a** and **1c** in pyridine-d_5 (δ in ppm, 500 MHz)[a]

C	1	1a	1c		C	1	1c
1	44.4 d	45.1 d	44.4 d	Glucose (inner)	1′	95.3 d	–
2	38.1 t	38.4 t	38.1 t		2′	74.0 d	–
3	172.2 s	176.5 s	174.3 s		3′	78.2 d	–
4	148.5 s	148.6 s	148.5 s		4′	70.9 d	–
5	47.6 d	48.0 d	47.6 d		5′	77.2 d	–
6	27.0 t	27.1 t	27.0 t		6′	69.5 t	–
7	32.1 t	32.3 t	32.1 t				
8	42.5 s	42.6 s	42.6 s	Glucose (central)	1″	105.1 d	–
9	52.0 d	52.0 d	51.9 d		2″	75.3 d	–
10	154.3s	154.0 s	154.4s		3″	76.4 d	–
11	28.4 t	28.5 t	28.5 t		4″	78.7 d	–
12	26.0 t	26.1 t	26.1 t		5″	78.0 d	–
13	39.3 d	39.5 d	39.5 d		6″	61.3 t	–
14	41.9 s	41.9 s	41.9 s				
15	31.1 t	31.3 t	31.3 t	Rhamnose (terminal)	1‴	102.7 d	–
16	32.1 t	32.7 t	32.7 t		2‴	72.6 d	–
17	57.1 s	56.7 s	56.7 s		3‴	72.8 d	–
18	49.5 d	49.4 d	49.4 d		4‴	74.1 d	–
19	47.2 d	47.5 d	47.6 d		5‴	70.3 d	–
20	150.7 s	151.2 s	151.2 s		6‴	18.5 q	–
21	31.0 t	31.3 t	31.3 t				
22	36.7 t	37.4 t	37.4 t	Glucose	1⁗	96.0 d	96.0 d
23	113.2 t	113.0 t	113.4 t		2⁗	74.2 d	74.3 d
24	22.3 q	22.5 q	22.4 q		3⁗	78.5 d	78.6 d
25	112.1 t	111.8 t	112.1 t		4⁗	71.1 d	71.2 d
26	15.3 q	15.3 q	15.3 q		5⁗	79.3 d	79.3 d
27	14.4 q	14.4 q	14.4 q		6⁗	62.2 t	62.3 t
28	175.0 s	178.9 s	178.9 s				
29	19.6 q	19.6 q	19.6 q				
30	110.0 t	109.9 t	109.9 t				

[a] Multiplicities were deduced from a DEPT experiment.

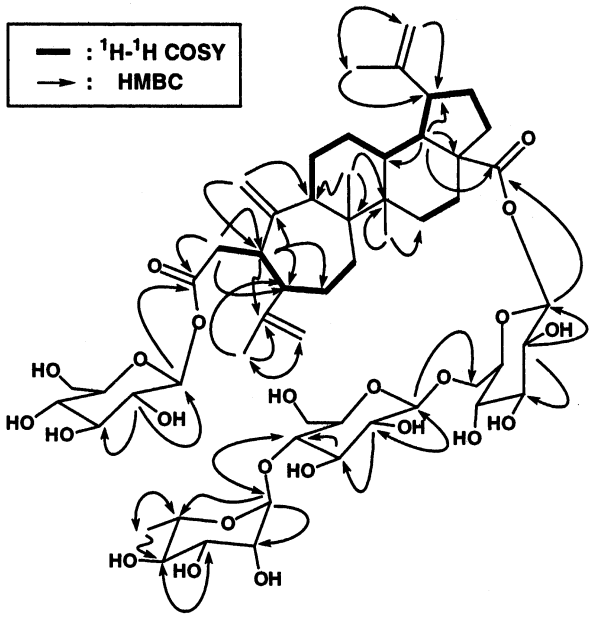

Figure 2. Selected ^{1}H–^{1}H COSY and HMBC for sachunoside (**1**).

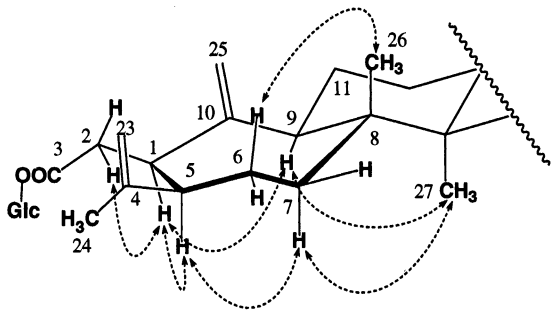

Figure 3. NOE correlations and the relative stereochemistry of sachunoside (**1**).

showed correlation to the methyl carbon at C-29 (δ 19.6) and methine carbon at C-19 (δ 47.5). Another set of exomethylene olefinic protons correlated to the methyl carbon at C-24 (δ 22.5) and the methine carbon at C-5 (δ 48.0). This evidence implied that the structure of **1a** was 3,4-*seco*-lup-4(23), 20(30)-diene type triterpene. The remaining set of exomethylene olefinic protons revealed the correlation to two methine carbons at C-1 and C-9 (Fig. 2). In the ^{1}H–^{1}H COSY and NOESY spectra, the presence of a cross-peak between H-1 and H-5 indicated that C_1 and C_5 were connected. On the basis of the above evidence, it was assumed that the six-membered B ring containing a C_5–C_{10} bond rearranged into the seven-membered B ring having a C_5–C_1 bond; thus the third exomethylene olefine group was settled to C_{25}=C_{10}. Therefore, sachunogenin (**1a**) was determined to be 3,4-*seco*-[(5-10)→(5-1)]-migrated-lup-4(23),10(25),20(30)-trien-3,28-dioic acid. All other data of 1D and 2D NMR spectra of the aglycon part supported the proposed structure. The configuration of the carboxymethyl group at C-1 was determined to be β-orientation on the basis of the NOESY as it showed cross peaks of H-1 with α-oriented H-9 and H-1 with H-5 (Fig. 3).

Acid hydrolysis of **1** afforded L-rhamnose and D-glucose as sugar moieties. In the HMBC spectrum, the anomeric proton (H-1′) of the inner glucose (δ 6.31) correlated with C-28 carboxylic carbon (δ 175.0), the anomeric proton (H-1″) of the central glucose (δ 4.93) with C-6′ of the inner glucose (δ 69.5), the anomeric proton of terminal rhamnose (δ 58.3) with C-4″ of the central glucose (δ 78.7), and the anomeric proton (H-1‴) of the other glucose (δ 6.32) with C-3 carboxylic carbon (δ 172.2) as illustrated in Fig. 2. Consequently, sachunoside (**1**) was determined to be 3-*O*-β-D-glycopyranosyl ester sachunogenin 28-*O*-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl ester.

With regard to the biosynthesis of **1**, the elimination of the hydroxyl group at C-1 (e.g. in compound **7**) would cause C_5–C_{10} bond migration into a C_5–C_1 bond.

Furthermore, compounds **2**–**8** were identified with chiisanoside,[12] 22-hydroxychiisanoside,[14] 1-de-hydroxychiisanoside,[7] isochiisanoside,[13] isochiisanoside methylester,[13] 11-dehydroxysochiisanoside[7] and inermoside,[7] respectively, on the basis of NMR and positive FABMS spectral data as known compounds (Fig. 4).

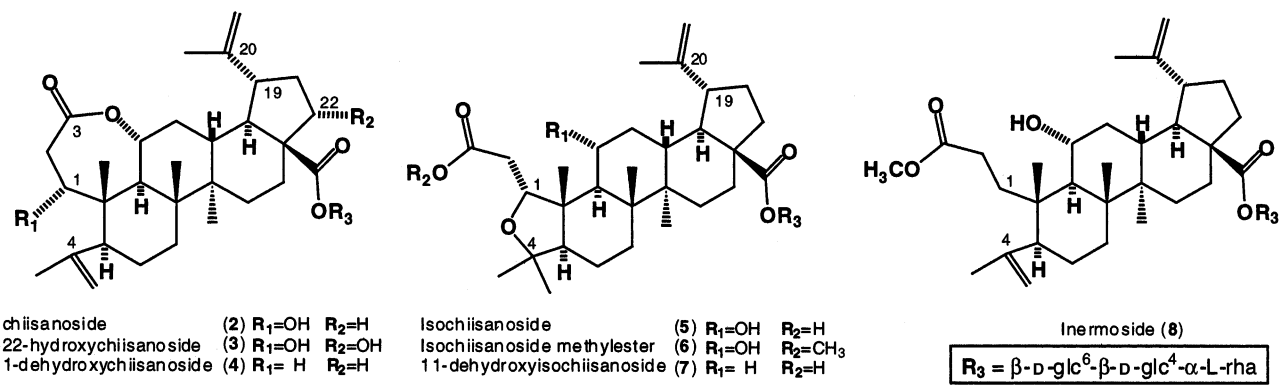

Figure 4. Structures of compounds **2**–**8**.

A 3,4-*seco*-lupane triterpene is rare in nature, and its glycosides are particularly characteristic in some *Acanthopanax* genera.[4–7,12–14] Sachonoside (**1**) especially attracts attention with respect to the 3,4-*seco*-migrated-lupane skeleton, possessing a new triterpene skeleton involving a seven-membered ring.

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8. Compound **1**: white powder, $[\alpha]_D$ −49.0 (*c* 0.55, MeOH), positive FABMS *m*/*z* 1123 ([M+Na]$^+$, $C_{54}H_{84}O_{23}$+Na), ^{1}H NMR (500 MHz, in pyridine-d_5) δ: 1.00 (3H, s, H-26), 1.02 (3H, s, H-27), 1.67 (3H, s, H-24), 1.71 (3H, s, H-29), 1.71 (3H, d, *J*=6.7 Hz, Rha H-6), 2.41 (1H, dd, *J*=5.5, 10.4 Hz, H-9), 3.04 (1H, ddd, *J*=7.9, 8.4, 8.5 Hz, H-1), 3.37 (1H, ddd, *J*=4.9, 10.5, 10.5 Hz, H-19), 4.71 (1H, s, H-30*a*), 4.80 (1H, s, H-25*a*), 4.85 (1H, overlapped, H-30*b*), 4.85 (2H, overlapped, H-23), 4.93 (1H, d, *J*=7.9 Hz, outer Glc H-1), 4.95 (1H, s, H-25*b*), 5.83 (1H, br s, Rha H-1), 6.31 (1H, d, *J*=7.9 Hz, inner Glc H-1), 6.33 (1H, d, *J*=7.9 Hz, glc H-1); anal. C, 54.45%, H, 7.90%, calcd for $C_{54}H_{84}O_{23}\cdot 5H_2O$, C, 54.35%, H, 7.73%.
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10. Compound **1a**: white powder, $[\alpha]_D$ −63.5 (*c* 0.46, MeOH), EIMS *m*/*z* (rel. int.): 422 [M−COOH−H]$^+$(14), 395[M−C_2H_4−COOH]$^+$ (100), 259 (44), 252 (22), 175 (28), 166 (40), 119 (29), 107 (30) ^{1}H NMR (500 MHz, in pyridine-d_5) δ: 1.00 (3H, s, H-26), 1.08 (3H, s, H-27), 1.74 (3H, s, H-24), 1.78 (3H, s, H-29), 2.54 (1H, dd, *J*=5.5, 10.4 Hz, H-9), 3.25 (1H, ddd, *J*=8.4, 8.4, 8.4 Hz, H-1), 3.54 (1H, ddd, *J*=4.3, 10.7, 10.7 Hz, H-19), 4.75 (1H, s, H-30*a*), 4.88 (1H, s, H-25*a*), 4.88 (1H, s, H-23*a*), 4.91 (1H, s, H-23*b*), 4.91 (1H, s, H-30*b*), 5.15 (1H, s, H-25*b*).
11. Compound **1c**: white powder, $[\alpha]_D$ −33.7 (*c* 0.89, MeOH), positive FABMS *m*/*z* 653 ([M+Na]$^+$, $C_{36}H_{54}O_9$+Na) EIMS *m*/*z* (rel. int.): 422 [M−COO−Glc]$^+$ (14), 409 [M−CH_2−COO−Glc]$^+$ (11), 395 [M−C_2H_4−COO−Glu]$^+$ (100), 259 (47), 252 (64), 175 (37), 166 (44), 107 (40), 73 (69) ^{1}H NMR (500 MHz, in pyridine-d_5) δ: 0.95 (3H, s, H-26), 1.06 (3H, s, H-27), 1.66 (3H, s, H-24), 1.79 (3H, s, H-29), 2.41 (1H, dd, *J*=7.9, 7.9 Hz, H-9), 2.70 (2H, d, *J*=7.9 Hz, H-2), 2.84 (1H, ddd, *J*=3.4, 12.5, 12.5 Hz, H-13), 3.06 (1H, ddd, *J*=7.7, 7.7, 7.7 Hz, H-1), 3.53 (1H, ddd, *J*=4.9, 10.7, 10.7 Hz, H-19), 4.76 (1H, s, H-30*a*), 4.79 (1H, s, H-25*a*), 4.84 (1H, s, H-23*a*), 4.85 (1H, s, H-23*b*), 4.92 (1H, s, H-30*b*), 4.96 (1H, s, H-25*b*), 6.35 (1H, d, *J*=8.5 Hz, Glc H-1)
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