TWO NEW CYCLOARTANE GLYCOSIDES FROM THALICTRI HERBA

Hitoshi YOSHIMITSU,[a] Kazuhiro HAYASHI,[b] Miki KUMABE[b] and Toshihiro NOHARA*,[b]

Faculty of Engineering, Kyushu Kyoritsu University,[a] 1-8 Jiyugaoka Yahata-nishi-ku, Kitakyushu 807, Japan and Faculty of Pharmaceutical Sciences, Kumamoto University,[b] 5-1 Oe-honmachi, Kumamoto 862, Japan

The structures of two cycloartane glycosides isolated from the methanolic extract of Thalictri Herba (Takatogusa), the dried aerial parts of *Thalictrum* sp. plants (Ranunculaceae), have been established on the basis of chemical evidence and spectroscopic means.

KEYWORDS Thalictri Herba; *Thalictrum* sp.; Ranunculaceae; cycloartane glycoside; thalictoside

Thalictrum sp. plants grow wild in Japan, and in their dried whole form, called Takatogusa, have been used as folk medicine for treating stomachache in the region of Nagano prefecture. We previously reported the structural characterization of two new cycloartane glycosides, thalictosides A and C,[1] isolated from the methanolic extract of the fresh aerial parts of *Thalictrum thunbergii* D.C. (Ranunculaceae). In an extended search for cycloartane type glycosides, we have now isolated two cycloartane glycosides, named thalictosides I and II, from the title crude drug. This paper describes their structural elucidation.

The water-soluble portion derived from the methanolic extract was subjected to column chromatography on Sephadex LH-20, ODS and silica gel to afford two new glycosides, designated thalictosides I (**1**) and II (**2**). Thalictoside I (**1**), a white powder, $[\alpha]_D$ +10.3° (MeOH), showed a $[M-H]^-$ peak at *m/z* 809 in the negative FAB-MS. The ^{1}H-NMR spectrum (pyridine-d_5) displayed an AB quartet signal at δ 0.29 and 0.88 ppm, which was characteristic of a cyclopropane methylene, five singlet methyl signals at δ 1.02, 1.26, 1.56, 1.68 and 1.70 ppm and a methoxy signal at δ 3.51 ppm. It also gave doublet and singlet signals at δ 5.03 and 6.74 ascribable to anomeric proton. Thus **1** was considered to be a cycloartane-type triterpene glycoside. This observation was supported by the ^{13}C-NMR data listed in Table I. The long-range COSY between two singlet olefinic methyl signals at δ 1.68 and 1.70 ppm and the olefinic proton (d, *J*=8.1 Hz) at δ 5.98 ppm indicated that the olefinic methyl groups attached to the same olefinic carbon and were located at the terminal of the side chain. In addition, a sequence of correlations in the olefinic proton at δ 5.98 ppm, an oxygen-bearing methine proton at δ 4.95 ppm, a hydroxy methine proton at δ 4.27 ppm, and a methine proton at δ 2.45 ppm, in turn, were observed in the ^{1}H-^{1}H COSY, and their signals could be assigned to the H-24, H-23, H-22 and H-20, respectively. Furthermore, the H-20 coupled both with a methine proton at δ 2.71 ppm due to H-17 and with a hemiacetal proton at δ 5.14 ppm due to H-21 which correlated to the methoxy proton at δ 3.51 ppm by long-range COSY. In addition, the NOE observations between H_3-18 and H-20, H-20 and H-23, H-20 and H-16, H-16 and H-22, and H_3-28 and H-17 suggested the stereo configuration for the structure of **1** to be as shown in Fig. 1. Moreover, with regard to the rings A, B, C and D, a comparative study of the ^{13}C-NMR spectrum of **1** with those of thalictosides A and C demonstrated C-30 to be a hydroxymethyl group. Other chemical shifts, except for the signals due to the side chain, C-17 on the D-ring and the sugar moiety, were coincident with them. On the other hand, acid hydrolysis with 2N hydrogen chloride in 50% dioxane gave unidentified artificial sapogenols derived from the genuine sapogenol along with D-glucose and L-rhamnose, whose absolute configurations were determined by gas-liquid chromatographic analysis as the trimethylsilyl ethers of their methyl 2-(polyhydroxyalkyl)-thiazolidine-4(*R*)-carboxylates.[2] To confirm the structure of oligosaccharide moiety, **1** was converted into the corresponding peracetate, **1**-peracetate, which showed fragment ion peaks at *m/z* 273 and 561 originating from the peracetylated

rhamnosyl and rhamnosyl glucosyl cations in the EI-MS. In the ^{1}H-NMR spectrum of the **1**-peracetate, NOE was detected between the anomeric proton (δ 5.02) of the peracetyl rhamnopyranosyl moiety and the H-2 (δ 3.72) of the triacetyl glucopyranosyl moiety, and between the anomeric proton (δ 4.55) of the peracetyl glucosyl moiety and the H-3 (δ 3.35) of the aglycone part. From the above evidence, the structure of **1** was concluded to be 21*S*, 22*R*, 23*R*-epoxy-21-methoxycycloart-24-en-3β, 22, 30-triol 3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside.

Thalictoside II (**2**), a white powder, $[\alpha]_D$ -32.2° (MeOH), showed the same ion peak due to $[M-H]^-$ as that of **1** at *m/z* 809 in the negative FAB-MS. The ^{1}H-^{1}H COSY of **2** disclosed signals due to one cyclopropane methylene [δ 0.34, 0.92 (each d, *J*=3.7 Hz, H_2-19)], three tertiary methyl groups [δ 0.99 (s, H_3-28), 1.06 (s, H_3-18) and 1.57 (s, H_3-29)], two olefinic methyl groups [δ 1.72 (s, H_3-26) and 1.74 (s, H_3-27)], one secondary methyl group [δ 1.75 (d, *J*=7.3 Hz, rha H_3-6)], one methine and one methylene groups [δ 1.77 (m, H-16β), 2.11 (m, H-20), 2.78 (m, H-17)], one methoxyl group at δ 3.39 ppm, two oxygen-bearing methine groups [δ 4.15 (br s, H-22), 4.89 (dd, *J*=8.8, 3.0 Hz, H-23)], one acetal proton [δ 5.05 (d, H-21)], two anomeric protons [δ 5.05 (d, glc H-1), 6.75 (s, rha H-1)], and one olefinic proton [δ 5.87 (d, *J*=8.8 Hz, H-24)]. A comparison of the ^{13}C-NMR spectrum of **2** with that of **1** showed shifts by -4.0, -2.3, -3.8, -1.7 and +1.6 ppm at C-17, C-20, C-21, C-22 and C-23, respectively, and the other signals were coincident. This observation was also supported by the ^{1}H-^{13}C COSY and long-range COSY. Moreover, the configurations of H-17α, 20*S*, 21*R*, 22*R*, 23*R* and the presence of the five-membered ring of the side chain were confirmed by the differential NOE measurement (Fig. 1). From the above evidence, **2** was revealed to be the epimer at C-21 of **1**. It has recently been reported that the analogous novel cycloartane compounds possessing the five-membered ring at the side chain were also isolated from *Monocyclanthus vignei* (Annonaceae).[3]

The occurrence of the acetal compounds, **1** and **2**, might be derived from that of the hemiacetal ones during the extraction procedure.

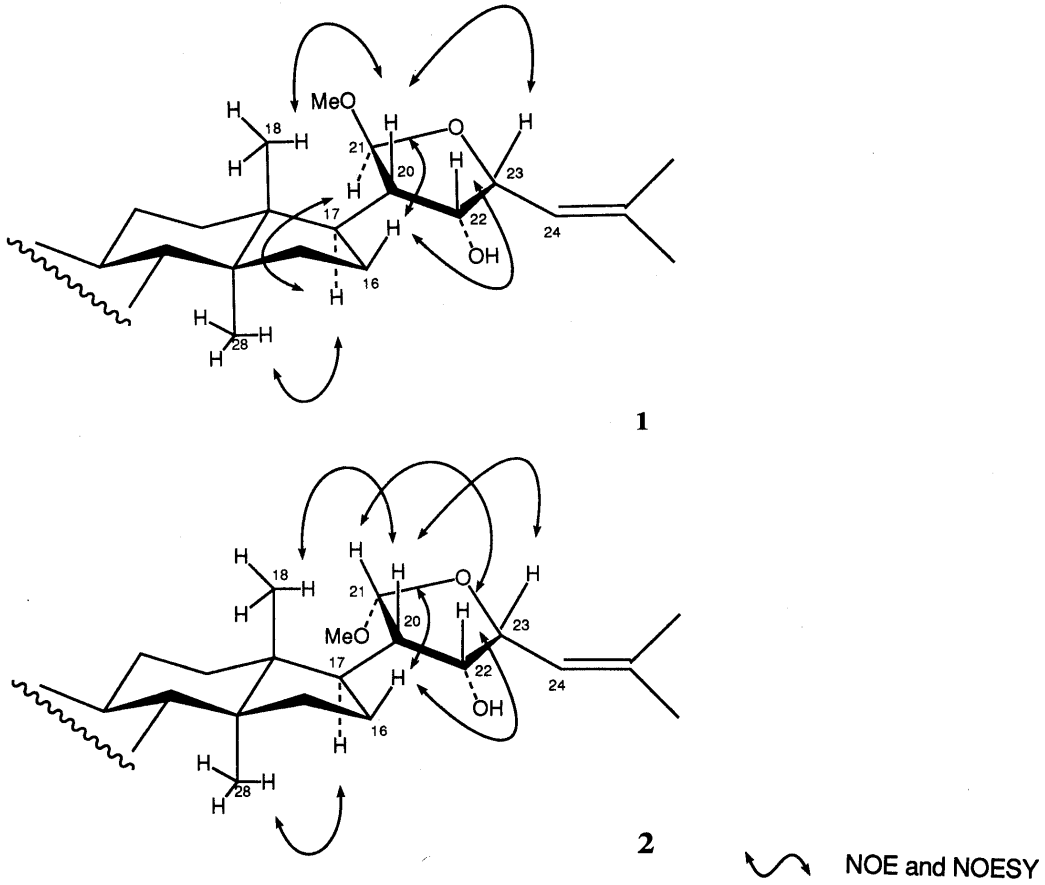
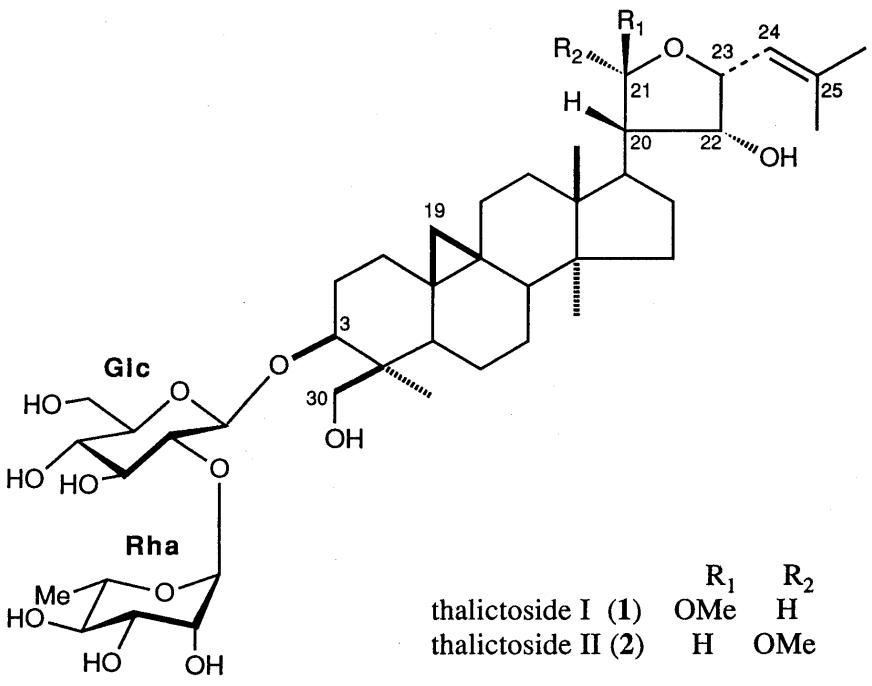


Fig. 1. NOE Experiments of **1** and **2**

Table I. ^{13}C-NMR Data for **1** and **2** (δ: ppm, in Pyridine-d_5)

	1	2		1	2		1	2
C- 1	30.8	31.5	C-16	26.7	26.9	OMe	55.5	54.6
2	29.9	29.9	17	44.7	40.7	glc C-1	105.4	105.4
3	89.3	89.3	18	18.6	19.5	2	80.3	80.3
4	45.3	45.3	19	29.8	29.7	3	76.3	76.3
5	47.6	47.4	20	54.8	52.5	4	72.4	72.4
6	22.6	22.5	21	108.7	104.9	5	78.2	78.2
7	27.7	27.0	22	76.7	75.0	6	62.8	62.8
8	48.2	48.2	23	79.0	80.6	rha C-1	100.2	100.9
9	20.1	20.1	24	122.7	123.7	2	71.9	72.0
10	26.4	26.5	25	136.1	135.9	3	72.1	72.1
11	26.6	26.6	26	26.0	26.0	4	74.5	74.4
12	35.7	35.8	27	19.7	19.6	5	69.1	69.1
13	45.5	45.3	28	18.6	18.6	6	18.5	18.4
14	48.8	48.8	29	19.9	19.9			
15	32.2	32.2	30	60.7	60.7			



	R_1	R_2
thalictoside I (**1**)	OMe	H
thalictoside II (**2**)	H	OMe

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REFERENCES AND NOTES

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