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LOGANIN AND A NEW IRIDOID GLUCOSIDE FROM *GENTIANA PYRENAICA*

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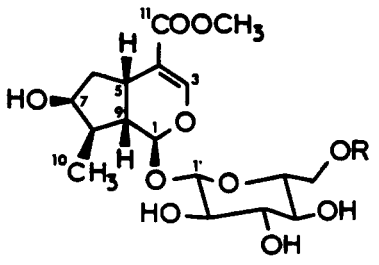
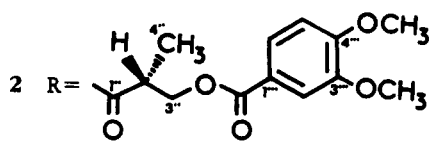
ABSTRACT.—6′-[2(*R*)-methyl-3-veratroyloxy propanoyl] loganin [**2**], a new iridoid glucoside has been isolated from the aerial parts of *Gentiana pyrenaica* along with the known loganin [**1**]. Their structures have been established by spectral and chemical means.

Gentiana pyrenaica L. (Gentianaceae) was previously reported to contain six flavonoids (1) and two phthalide glucosides (2). Continuing the investigation for the chemical constituents of this species, the monoterpene components were studied. Herein we describe the isolation and characterization of 6′-[2(*R*)-methyl-3-veratroyloxy propanoyl] loganin [**2**], a new iridoid glucoside obtained from the aerial parts of this species along with the known iridoid loganin [**1**]. Their structures were determined by spectral and chemical evidence. This is the first time that iridoid glucosides are reported from *G. pyrenaica*.

Dried and powdered aerial parts of *G. pyrenaica* were extracted as described elsewhere (2). Chromatographic purification of the $CHCl_3$ extract by centrifugal tlc, polyamide cc, and hplc afforded compounds **1** and **2**.



1 R=H



2 R=

Loganin [**1**] was identified by spectral and chromatographic comparison with an authentic sample and with literature values (3).

Compound **2** showed a positive vanillin reaction identical to that of **1**, suggesting it to be an iridoid. In addition to the 240 nm absorption typical of a methoxycarbonyl enol ether system, the uv spectrum of **2** displayed two peaks at 255 and 290 nm indicating the presence of a phenolic acid unit in the molecule. Besides the typical loganin resonances, the ^{1}H-nmr spectrum exhibited signals of a 1,3,4-trisubstituted aromatic ring with two methoxyl groups characteristic of a veratroyl moiety (4). This one was in accordance with fabms data which showed fragments at *m/z* 165 (fab^+) and *m/z* 181 (fab^-). The ^{1}H-nmr spectrum, completed by spin decoupling experiments, displayed further signals corresponding to a β-hydroxyisobutyroyl unit (5). The chemical shift value of both the H-3″A and H-3″B (4.43 and 4.36 ppm) indicated that this unit was acylated at C-3″ with veratric acid. This result was in agreement with fab^+ms which showed two ions at *m/z* 251 and 268 arising from the β-hydroxyisobutyric acid esterified with veratric acid. Evidence for location of the latter fragment at C-6′ of the glucose

was given by the downfield shift of the C-6′ methylene signals in the ^{1}H- and ^{13}C-nmr spectra. As expected, alkaline hydrolysis of **2** afforded loganin, veratric acid, and β-hydroxyisobutyric acid; the latter had a negative optical rotation {$[\alpha]^{25}D$ −25° (c = 0.105, MeOH)} indicating that it had the *R* configuration (6). From the above data compound **2** was characterized as 6′-[2(*R*)-methyl-3-veratroyloxy propanoyl] loganin, a new natural product.

In the family Gentianaceae, loganin derivatives were first isolated from *Gentiana pedicellata* (3,7) which like *G. pyrenaica* belongs to the Chondrophylla section. However, these iridoid glucosides differ from those of *G. pyrenaica* by the acylating unit and by its location on the glucose.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—General isolation methods and instrumentation were similar to those used for the analysis of *G. pedicellata* (3). ^{1}H- and ^{13}C-nmr spectra were obtained, respectively, on a Bruker AM 400 and AM 300 with TMS as internal standard. Fabms spectra were recorded on a Nermag R 10-10C.

ISOLATION.—Dried and powdered aerial parts of *G. pyrenaica* (240 g) were extracted as reported previously (2). $CHCl_3$ extract (7 g) was chromatographed by Si gel centrifugal tlc eluting by $CHCl_3$/MeOH with increasing MeOH content. Fractions eluted with $CHCl_3$-MeOH (9:1) were fractionated by polyamide cc [C_6H_6-MeOH (97:3)] yielding **2** (10 mg) after purification using RP-18 hplc [MeOH-H_2O (55:45)]. Compound **1** (2 mg) was obtained from the fraction eluted with $CHCl_3$-MeOH (6:4) and purified by RP-18 hplc [MeOH-H_2O (65:35)].

LOGANIN [**1**].—Identified by comparison of tlc, hplc, and ^{1}H- and ^{13}C-nmr spectra with authentic sample and literature values (3).

COMPOUND **2**.—Colorless amorphous powder: $[\alpha]^{25}D$ −32° (c = 0.80, MeOH); uv λ max (MeOH) 225, 240, 255, 290; fab$^+$ms $[M+Na]^+$ 663, $[M+H]^+$ 641, $[M-aglycone]^+$ 413, 268, 151, 165; fab$^-$ms $[M-H]^-$ 639, 181, [M − glc acylated]$^-$ 227; ^{1}H and ^{13}C nmr see Table 1.

ALKALINE HYDROLYSIS OF **2**.—Compound **2** (8 mg) was dissolved in 1 ml MeOH and 1 ml 1N NaOH. After 1 h at room temperature the reaction mixture was neutralized with HCl and extracted with $CHCl_3$ and EtOAc. The $CHCl_3$ and EtOAC layers afforded, respectively, veratric acid and β-hydroxyisobutyric acid, both identified by comparison of their spectral data (^{1}H nmr) with authentic samples. The aqueous layer yielded loganin identified by comparison with a sample by tlc and hplc (in the above conditions loganic acid was not detected).

TABLE 1. ^{1}H- and ^{13}C-nmr data (400/75 MHz, CD_3OD) of compound **2**.

Position	^{1}H[a]	^{13}C
1	5.06 d (5)	98.3
3	7.34 d (1.5)	150.3
4	—	113.9
5	3.08 m	32.5
6a	1.51 ddd (14,8.5,5)	42.9
6b	2.22 ddd (14,7.5,1.5)	
7	3.99 m	74.9
8	1.81 dqd (9,7,5)	42.4
9	1.94 td (9,5)	46.5
10	1.04 d (7)	13.8
11	—	169.5
11-OMe	3.67 s	51.6
1′	4.59 d (8)	100.3
2′	3.18 dd (9,8)	74.8
3′	3.30–3.35 m	77.7
4′		71.7
5′	3.48 ddd (9,6.5,2)	75.8
6′a	4.59 dd (12,2)	64.9
6′b	4.18 dd (12,6.5)	
1″	—	175.2
2″	2.99 quint. d (7,5.5)	40.8
3″a	4.43 dd (10.5,7)	67.0
3″b	4.36 dd (10.5,5.5)	
4″	1.23 d (7)	14.1
Ar-CO	—	167.5
1‴	—	123.5
2‴	7.50 d (2)	113.6
3‴	—	150.3
4‴	—	155.1
5‴	7.02 d (8)	112.2
6‴	7.63 dd (8,2)	125.0
OMe	3.89–3.87 2s	56.6

[a]Values in parentheses are coupling constants in Hz.

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