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IRIDOID GLYCOSIDES FROM *EUCNIDE BARTONIOIDES*

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Key Word Index—*Eucnide bartonioides*; Loasaceae; iridoid glycosides; morroniside; kingiside; sweroside; secologanol; 8-*epi*-loganin; loganin; 5-hydroxyloganin.

Abstract—*Eucnide bartonioides* yielded morroniside as the main iridoid constituent. In addition, six minor iridoid glucosides were isolated namely the known glucosides: kingiside, sweroside, secologanol, 8-*epi*-loganin and loganin as well as a novel iridoid glucoside, which by spectroscopic methods was assigned to be 5-hydroxyloganin. The compound 8-*epi*-loganin has so far been reported only from Scrophulariaceae and related families and it is rather unexpected in Loasaceae.

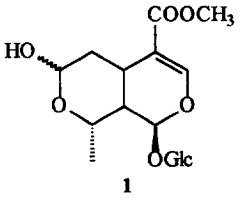
INTRODUCTION

The taxonomic position of Loasaceae has for a long time been a matter of controversy. Thus, Thorne [1] has placed this family in its own order near Myrtales, Cronquist [2] preferred the more traditional position in Violales while Dahlgren believed in an affinity to his Cornales-Dipsacales complex as well as to Gentianales [3], mainly due to the embryological characters together with the presence of iridoids in the family [4]. Previous chemical work on these compounds has been done mainly on *Mentzelia* [5–9] although iridoids have been reported from other genera too [10–13]. In continuation of our research on iridoid glycosides from Loasaceae, we have now examined *Eucnide bartonioides* Zucc. To our knowledge, no previous phytochemical study of this genus has been reported.

RESULTS AND DISCUSSION

The water-soluble part of an ethanolic extract of *E. bartonioides* was fractionated by reverse phase chromatography to give as the major compound morroniside (**1**), seen in the ^{1}H NMR spectrum as a mixture of the anomeric forms [14]. Minor constituents were kingiside (**2**), sweroside (**3**), 8-*epi*-loganin (**4**), an unknown (**5**), secologanol (**6**) and loganin (**7**).

The ^{13}C NMR spectrum of **5** (Table 1) contained 17 signals of which six could at once be assigned to a β-glucopyranosyl moiety. The remaining 11 signals fitted well with a loganin-like structure, including the secondary hydroxyl group but with an additional tertiary hydroxyl substituent (δ 72.9) which therefore had



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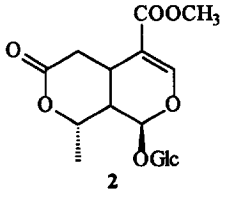

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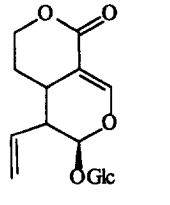

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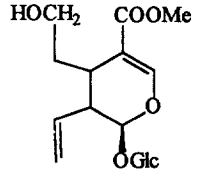

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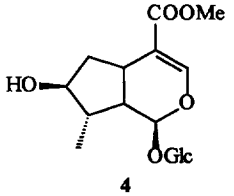

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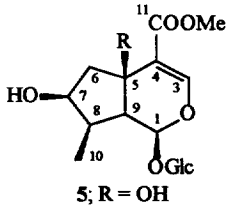
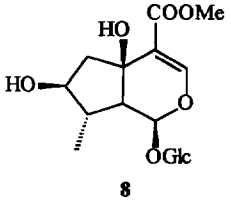


5; R = OH
7; R = H



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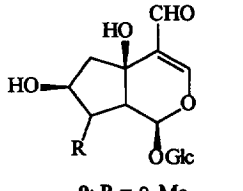

9; R = β-Me
10; R = α-Me

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Table 1. ^{13}C NMR data for iridoid glucosides in CD_3OD

C	5	8*	9†	10‡
1	96.0	95.68	97.12	96.5
3	152.4	153.43	162.70	164.0
4	115.4	115.26	126.78	126.4
5	72.9	71.47	72.12	70.4
6	49.0	48.05	48.88	46.8
7	74.4	77.93	73.38	77.7
8	41.4	43.57	41.23	43.0
9	55.0	51.56	54.72	51.1
10	13.1	13.84	13.14	13.9
11	168.2	168.07	192.95	192.5
1′	99.9	99.68	100.12	98.8
2′	73.5	74.41	74.37	74.2
3′	77.6	77.54	78.43	77.3
4′	71.6	71.73	71.54	71.5
5′	78.5	78.41	77.55	78.4
6′	62.7	62.84	62.69	62.7
OMe	51.6	51.62	—	—

* Data from ref. [16].
† Data from ref. [17].
‡ Data from ref. [18].

to be situated at C-5 or C-8. The ^1H NMR spectrum of **5** showed a singlet for the 11-carbomethoxy group at δ 3.72. Another singlet at δ 7.40 was assigned to H-3 and proved that the carbon atom at C-5 must be completely substituted. The doublet nature of the C-10 methyl group at δ 1.10 further showed that the second hydroxy group was not at C-8. The coupling pattern allowed assignment of all the signals from H-6 through H-9 and H-1 (see Experimental), proving the position of the secondary hydroxyl group to be at C-7. This was in agreement with the overall structure **5**. Assuming the usual configuration at C-1, C-5 and C-9, only the stereochemistry at C-7 and C-8 remained to be established. One compound with the same gross structure is known, namely auroside (**8**) isolated from *Phlomis aurea* [15]; however, no data were reported. Fortunately, **8** has been prepared synthetically [16], and NMR data were thus available (Table 1) to show the non-identity of **5** and **8**. Other compounds with a similar structure are known, namely the 8-epimeric pair tecomoside/*epi*-tecomoside (**9/10**), both with a C-11 aldehyde function [17, 18]. Comparison of the ^{13}C NMR spectra of **5** and **8** with those of the pair **9/10** (particularly the shift values for C-7, C-8 and C-9) showed that **5** and **8** had to be epimeric at C-8, too. It is significant that the C-9 resonances in **5** and **9** with a β-methyl group at C-8 are more low field (δ 55) than those of **8** and **10** with the α-methyl group (δ 51) [17]. Furthermore, comparisons of the coupling constants for the protons of the cyclopentane ring in compounds **5/8** and **9/10** confirm the relative configuration to be 8β-methyl in compound **5** (see Table 2). Particularly, the large size of $J_{8,9}$ (12 Hz) show that H-8 and H-9 are in a transdiaxial position in **5** and **8**.

Table 2. Coupling constants for the protons of the cyclopentane ring in compounds **5** and **8–10**

Compound	$J_{1\beta,9\beta}$	$J_{6\alpha,7\alpha}$	$J_{6\beta,7\alpha}$	$J_{7\alpha,8\alpha}$	$J_{8\alpha,9\beta}$	$J_{8\beta,9\beta}$
5	2.0	5.6	2.7	5.1	12.0	—
8*	1.6	6.7	5.6	§	—	10.3
9†	1.7	5.8	2.7	5.8	12.0	—
10‡	1.1	5.6	7.3	§	—	10.8

* Data from ref. [16].
† Data from ref. [17].
‡ Data from ref. [18].
§ No data given.

Within Loasaceae, *Eucnide* has been connected with *Mentzelia* and *Schismocarpus* in the subfamily Mentzelioideae [17]. The carbocyclic iridoids found in *E. bartonioides* are similar to schismoside isolated from *Schismocarpus matudai* [12], but different from the compounds isolated from the genus *Mentzelia*. Apparently, this genus is the only one in the family which contains iridoids lacking C-10. However, both types of iridoids can be presumed to be biosynthetically derived from iridodial with the 8β-stereochemistry [12, 20]. The finding of 8-*epi*-loganin in Loasaceae is unexpected since compounds with the 8α-methyl stereochemistry have so far been restricted to the Scrophulariales/Lamiales complex. We do not consider this compound to have taxonomic significance, since the remaining compounds (including the secoiridoids) all belong biosynthetically to the 8β-series which is characteristic for Cornales/Dipsacales and Gentianales.

EXPERIMENTAL

General procedures. Mps. uncorr.; ^1H and ^{13}C NMR: CD_3OD at 250 and 63 MHz, respectively, (the solvent peak was used as int. standard). Prep. TLC: 20 × 40 cm plates coated with 1 mm layers of Silica Gel PF_{254} (Merck); bands were detected in UV light (254 nm); Reverse phase MPLC: Merck Lobar C-18 columns size B and C. H_2O–MeOH mixts were used as eluents and peaks were detected by UV at 210 nm.

Plant material. Eucnide bartonioides was grown by The Botanical Garden of Copenhagen at the field station at Tåstrup. (The voucher IOK 25-96 was deposited at The Botanical Museum, The University of Copenhagen and identified by Dr Bertel Hansen). It was either used fresh or frozen in polyethylene bags and kept at −23°.

Isolation of iridoids. Fresh whole plants (142 g) were extracted with EtOH (2 × 0.4 l), filtered, taken to dryness and partitioned in H_2O–Et_2O. The aq. layer was concd, redissolved in MeOH and treated with activated charcoal. Evapn of the filtrate gave a white foam (4 g), which was subjected to MPLC (C-column) eluting with H_2O–MeOH mixts (10:1 to 2:1). This gave (in order of elution) kingiside (**2**; 12 mg), morroniside (**1**; 509 mg, 0.35%), sweroside (**3**; 10 mg), a

mixture of **4** and **5** (20 mg), secologanol (**6**, 20 mg) and loganin (**7**; 10 mg). The above mixt. was sepd. by prep. TLC ($CHCl_3$–MeOH; 3:1) to give 8-*epi*-loganin (**4**) (5 mg) and 5-hydroxyloganin (**5**; 10 mg). The known compounds were identified by comparison of the NMR spectra with those of authentic samples.

5-Hydroxyloganin (**5**). $[\alpha]_D^{21} -88°$ (MeOH; *c* 0.6); UV λ_{max}^{MeOH} nm: 232; MS *m/z* (rel. int.): 424 $[M+NH_4]^+$ (0.04), 406 $[M+NH_4-H_2O]^+$ (0.07), 191 $[M-Glu-2H_2O]^+$ (100); ^1H NMR (CD_3OD): δ 7.40 (*s*, H-3), 5.63 (1H, *d*, $J = 2.0$ Hz, H-1), 4.57 (1H, *d*, $J = 8.0$ Hz, H-1′), 3.92 (1H, *ddd*, $J = 5.6$, 5.1 and 2.7 Hz, H-7), 3.89 (1H, *dd*, $J = 12.0$ and 1.8 Hz, H_a-6′), 3.72 (3H, *s*, COOMe), 3.67 (1H, *dd*, $J = 12.0$ and 5.2 Hz, H_b-6′), *ca* 3.3 (3H, H-3′, H-4′ and H-5′), 3.18 (1H, *dd*, $J = 9.0$ and 8.0 Hz, H-2′), 2.47 (1H, *dd*, $J = 15.0$ and 5.6 Hz, H_a-6), 2.33 (1H, *dd*, $J = 12.0$ and 2.0 Hz, H-9), 2.16 (1H, *dd*, $J = 15.0$ and 2.7 Hz, H_b-6), 1.67 (1H, *ddq*, $J = 12.0$, 5.1 and 7.0 Hz, H-8), 1.10 (3H, *d*, $J = 7.0$ Hz, 10-CH_3); ^{13}CNMR: Table 1.

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