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IRIDOID GLUCOSIDES FROM *PICCONIA EXCELSA*

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Key Word Index—*Picconia excelsa*; Oleaceae; iridoid glucosides; secoiridoid glucosides; picconiosides I, II, III, IV, and V; loganic acid; loganin; 7-ketologanic acid; 7-ketologanin; 6β-hydroxy-7-*epi*-loganin; 8-*epi*-kingisidic acid; 8-*epi*-kingiside; secoxyloganin; oleoside 11-methyl ester; ligstroside; excelsioside; verbascoside; oleoacteoside.

Abstract—An investigation of the iridoids of *Picconia excelsa* from Tenerife provided 17 iridoid glucosides together with verbascoside. Major constituents (> 0.5%) were loganin, ketologanin, oleoacteoside and the new picconioside I—a bisiridoid consisting of loganin esterified with deoxyloganin. Minor constituents were secoxyloganin, 8-*epi*-kingiside, 8-*epi*-kingisidic, oleoside 11-methyl ester, excelsioside, ligstroside and loganic acid together with the new compounds ketologanic acid, 6β-hydroxy-7-*epi*-loganin and picconiosides II–V, the latter four being esters of loganin and menthiafolic, foliamenthic, 6-(*Z*)-foliamenthic or 6,7-dihydrofoliamenthic acid. The structures were mainly elucidated by NMR spectroscopy. © 1997 Elsevier Science Ltd. All rights reserved

INTRODUCTION

The genus *Picconia*, which contains only two species, is restricted in its geographical distribution to the Canary Islands, Madeira and the Azores. Systematically, *Picconia* has been considered a probable relative to *Phillyrea* [1], and this is consistent with the similar flavonoid contents in *Picconia excelsa* and *Phillyrea latifolia* [2]. No previous work concerning the iridoids in the genus has been reported. In connection with our on-going investigation of these compounds in Oleaceae [*cf.* 3, 4], we have now undertaken an investigation of *P. excelsa* (Ait.) DC.

RESULTS AND DISCUSSION

Dried, powdered foliage was extracted with ethanol, and the resulting extract was partitioned between water and ether. The water-soluble part was subjected to further solvent partitioning between water and ethyl acetate. Reverse phase chromatography of the two fractions allowed the isolation of altogether 17 iridoid glucosides.

Several carbocyclic iridoids were isolated from the water-soluble extract, namely the major constituents loganin (**1**) and 7-ketologanin (**2**); whereas 6β-hydroxy-7-*epi*-loganin (**3**), loganic acid (**4**) and 7-ketologanic acid (**5**) were only minor components. Of these, **3** and **5** have not previously been isolated as natural plant constituents, although both have been synthesized [4, 5]. The known secoiridoids secoxyloganin (**6**) [6], 8-*epi*-kingiside (**7**) [7], 8-*epi*-kingisidic acid (**8**) [8] and oleoside 11-methyl ester (**9**) [9, 10] were found as minor constituents. Both verbascoside (**10**), oleoacteoside (**11**) [11] and a new bisiridoid glucoside, named picconioside I (**12**), were less polar major components in the water-soluble extract. In the ethyl acetate fraction, the main components were **10**, excelsioside (**13**) [10], ligstroside (**14**) [10, 12] and **12**, followed by four hitherto unknown acyclic monoterpene esters of loganin, which we have named picconiosides II–V (**15**–**18**).

The new compounds **3** and **5** were both isolated in small quantities. The identity of 7-ketologanic acid (**5**) was proved by comparison with an authentic sample prepared by saponification of **2** [4]. The ^{13}C NMR spectrum of **3** showed the usual 17 signals of a carbocyclic iridoid like loganin. However, in addition to the sugar signals, two peaks at δ 84.3 and 85.8 indicated the presence of two -CHOH- functionalities in the cyclopentane ring (and this could therefore only be C-6 and C-7). Furthermore, the lowfield chemical shifts indicated a *trans*-relationship between the hydroxy groups. The four possible 6,7-stereoisomers of 6-hydroxyloganin have been synthesized [5], and comparison of the ^1H NMR spectrum of **3** with those

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Table 1. ^{13}C NMR data (125 MHz, CD_3OD) of picconiosides I–V (and their acetates in $CDCl_3$) and model compounds

C	12	19	20	15	16/17	18	12a	15a	16a/17a	18a
1a	97.5		97.6	97.3	97.4	97.4	94.4	94.4	94.4	94.3
3a	152.6		152.6	152.5	152.5	152.5	149.2	148.7	148.7	148.7
4a	113.2		113.1	113.1	113.1	113.2	113.4	113.6	113.6	113.6
5a	32.6		32.7	32.5	32.5	32.5	29.6	29.6	29.6	29.6
6a	40.5		40.3	40.4	40.4	40.4	38.7	38.9	38.8	38.7
7a	78.1		78.6	78.6	78.7	78.7	76.3	76.9	76.9	76.8
8a	40.9		40.8	40.9	40.9	41.0	38.8	38.8	38.7	38.8
9a	47.1		47.0	47.1	47.1	47.1	45.5	45.8	45.4	45.4
10a	13.8		13.6	13.7	13.7	13.7	12.4	12.3	12.3	12.2
11a	169.3		169.3	169.2	169.2	169.3	166.8	167.3	167.2	167.3
Me	51.8		51.7	51.8	51.8	51.7	51.0	51.0	51.0	51.0
1b	97.9	97.9	172.6	169.1	168.9 168.9	169.2	95.3	166.9	166.8 166.8	166.8
2b			21.0	128.7	129.3 129.0	128.7		127.6	128.2 128.0	127.5
3b	152.6	152.7		144.0	142.9 143.2	144.0	148.8	142.2	141.2 141.2	142.1
4b	113.2	112.9		27.5†	28.1 27.8	27.1	113.1	27.8	27.1 26.7	25.9
5b	35.1	35.3		41.7	31.5 39.1	36.9	32.2	40.5	30.8 37.8	35.4
6b	33.5	33.4		73.5	138.5 138.2	30.5	31.2	72.8	140.8 140.7	29.5
7b	34.2	34.2		145.8	126.5 125.8	40.5	32.9	144.4	119.9 118.9	35.1
8b	36.6	36.6		112.5	59.1 59.3	60.9	34.8	112.0	61.0 60.5	62.4
9b	49.1	49.3		12.5	12.5 12.5	12.5	47.9	12.1	12.3 12.2	12.1
10b	20.7	20.9		24.5†	23.5 16.2	19.7	19.2	23.2	23.2 16.2	19.0
11b	168.8	169.7					166.1			
1′	100.1*	100.2	100.2	100.0	100.1	100.1	96.0 95.7	95.6	95.6	95.6
2′	74.7*	74.8	74.7	74.6	74.6	74.6	70.4 70.4	70.4	70.4	70.4
3′	77.9*	78.1	78.0	77.8	77.8	77.9	72.0 71.8	72.0	72.0	72.0
4′	71.5*	71.6	71.6	71.5	71.5	71.5	68.1 68.0	68.0	68.0	68.1
5′	78.3*	78.4	78.4	78.2	78.2	78.3	72.4 72.3	72.3	72.2	72.2
6′	62.7*	62.8	62.8	62.7	62.7	62.7	61.6 61.5	61.5	61.5	61.5

* Denotes double intensity of signal.
† Signals have been interchanged [15].

of the above stereoisomers showed that **3** was 6β-hydroxy-7-*epi*-loganin. Another stereoisomer, 6β-hydroxyloganin, has been isolated from *Fouquieria columnaris* (Fouquieriaceae) [13].

Picconioside I (**12**) was a major constituent both in the water- and the ethyl acetate-soluble fraction. The ^{13}C NMR spectrum (Table 1) showed the presence of 33 carbon atoms including signals from two β-glucopyranosyl moieties (seen as six peaks of double intensity). The other signals corresponded to two iridoid aglucones with 10 and 11 carbons, respectively, indicating **12** to be a bisiridoid glucoside connected by an ester bond not involving the sugar residues. Thus, one set of signals (the b-part) which closely resembled the spectrum of deoxyloganin (**19**) could be distinguished. The remaining set of signals (the a-part) was similar to the spectrum of loganin (**1**), except for minor chemical shift differences for C-6, C-7 and C-8, indicating the bridging ester bond to be located at the 7-position of the loganin moiety. Consequently, we prepared 7-*O*-acetyl-loganin (**20**) by partial deacetylation of loganin pentaacetate (see Experimental) and comparison of the ^{13}C NMR spectra of **20** and the a-part of **12** revealed a very close fit. This was consistent with the ^1H NMR data where H-7 was seen at δ 5.19 and 5.20 in **12** and **20**, respectively, and with the remaining signals in the spectrum of **12** being almost coincident partly with those of **19** and partly with those of **20**. Acetylation of **12** yielded an octaacetate (**12a**) in accordance with the proposed bisiridoid structure. Final proof was obtained by saponification of **12** to give loganic acid (**4**) and deoxyloganic acid (**21**). A similar bisiridoid consisting of two loganin moieties (ligustrinoside) also linked through a C-7a to C-11b ester bond has been reported from *Strychnos ligustrina* (Loganiaceae) [14].

According to the ^{13}C NMR spectra, picconiosides II–V (**15–18**) each contained 27 carbon atoms, of which 17 could be assigned to a loganin moiety esterified at C-7 as seen in **12** (Table 1). The remaining 10 signals in each compound appeared to be attributable to four different acid residues of monoterpenoid origin and all with a 2,3-double bond (and all with an *E*-configuration—see below). The NMR spectra of picconioside II (**15**) showed, besides the above-mentioned loganin moiety (a-part), signals consistent with a menthiafoloyl substituent (listed in Table 1 as carbons 1b–10b). Furthermore, comparison with the NMR spectra of the recently reported jashemsloside A (isolated from *Jasminum hemsleyi* [15]) revealed

identity. However, a significant difference in the optical rotations was observed ($-29°$ vs $-36°$ for **15** and jashemsloside A, respectively) and this showed that the ratio 6b(*S*):6b(*R*) is higher in **15** from *Picconia* since the (*S*)-isomer of the methiafoloyl moiety gives a positive contribution to the overall optical rotation [15]. A number of other iridoids containing a menthiafoloyl moiety have been reported, namely menthiafolin from *Menyanthes trifoliata* (Menyanthaceae) [16, 17], kickxioside from *Kickxia spuria* [18], lamourouxide from *Lamourouxia multifida* [19] and ambiguuside from *Penstemon ambiguus* (all Scrophulariaceae) [20]. Also, menthiafolic acid residues are present in monoterpene glucosides found in *Viburnum* spp. (Caprifoliaceae) [21–23].

Picconiosides III and IV (**16** and **17**) were isolated as an apparently inseparable isomer mixture (*ca.* 2:1) with very similar ^{1}H and ^{13}C NMR spectra (Table 1). From the ^{1}H NMR spectrum (see Experimental), it could be deduced that both compounds contained a loganin moiety esterified with a mixture of foliamenthic acid and its 6b-(*Z*)-isomer (Scheme 1). To determine which derivative was the predominant component in the mixture, a comparison with ^{13}C NMR data of similar esters were performed. Recently, the corresponding 6-acylated catalpol derivatives, namely nemoroside [20, 24] and 6″(*Z*)-nemoroside [20] were isolated from *Penstemon ambiguus* as two separable compounds [20], and the ^{13}C NMR data of the acid moieties of this pair deviated less than 1.0 ppm from the values observed in the pair **16/17**. Thus, the most abundant isomer was determined to be **16** with a 6b-(*Z*)-foliamenthoyl side-chain. As previously noted by Stermitz *et al.* [20], the only major ^{13}C NMR differences between such nerol (6-(*Z*)) and geraniol (6-(*E*)) derived side-chains appear for C-5b and C-10b (see numbering in Scheme 1). Hence, if we consider the chemical shift difference between C-5b and C-10b ($= \Delta_{5\text{-}10}$), a convenient general rule might be expressed as: $\Delta_{5\text{-}10} < 10 \rightarrow$ (*Z*)-configuration of the 6b,7b-double bond (i.e. nerol derived), whereas $\Delta_{5\text{-}10} > 20 \rightarrow$ (*E*)-configuration of the 6b,7b-double bond (i.e. geraniol derived). When applied to the above pairs the values 7.0 ppm vs 22.9 ppm were obtained, while 6-*O*-nerol-8-oyl-antirrinoside (from *Anarrhinum orientale* [25]) gives $\Delta_{5\text{-}10} = 7.3$ ppm, and the geraniol derived nemorososide (from *Penstemon nemorosus* [24]), 6-β-*O*-(2,8-dimethyl-[2*E*,6*E*]-octadienoyl)-boschnaloside (from *Penstemon virens* [26]), 6-*O*-(2,8-dimethyl-[2*E*,6*E*]-octadienoyl)-penstemoside (from *Penstemon cyathophorus* [26]), amareloside (from *Tecoma chrysantha*, Bignoniaceae [27]), and glycosyl 8-hydroxy-2,6-dimethyl-(2*E*,6*E*)octadienoate (from *Radermachia sinica*, Bignoniaceae [28]) had $\Delta_{5\text{-}10} = 22.0$, 22.4, 22.3, 24.8 and 22.9 ppm, respectively. The above geraniol derived acid also occurs in the secoiridoid, foliamenthin (from *Menyanthes trifoliata*, [16]) and in the glucosyl esters, 5″-hydroxydigipenstroside and penstriasoside [from *Penstemon digitalis* (Scrophulariaceae) [29]].

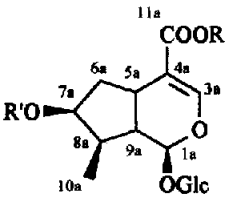
The NMR spectra of the last ester, picconioside V (**18**), showed, besides the loganin unit, the presence of an acid moiety derived from citronellol (6,7-dihydrofoliamenthic acid). Comparison with published spectra of two derivatives of 6,7-dihydrofoliamenthic acid, namely the 1-β-D-glucopyranosyl ester [32] and the methyl ester [33], revealed a remarkably close fit with **18**, confirming the proposed structure. This left only the chiral centre at C-6b in **18** to be determined. Since only one set of ^{13}C NMR signals was seen for the acyclic monoterpene part, this might indicate homogeneity of the product. However, the influence of the distant asymmetric C-6b on the iridoid part is likely to be insignificant (*cf.* the geometric isomers **16/17**), and thus not observable in NMR, therefore the compound might in fact well be a mixture of 6b-epimers. An attempt to cleave **18** in sodium methoxide at room temperature failed and at elevated temperature (50°) decomposition took place. Due to the limited amount of compound available no further attempts at determining the absolute configuration at C-6b were made. Known derivatives of 6,7-dihydrofoliamenthic acid are the diglycosidic macrolides urceolide and lonitoside from *Viburnum urceolatum* [30] and *Lonicera nitida*, [31], respectively (both Caprifoliaceae). Moreover, two acyclic glucosyl derivatives of this acid have been reported from *Sambucus ebulus*, (Caprifoliaceae) [32] and from *Linaria japonica*, (Scrophulariaceae) [33]. Except for the last example, all these compounds have been shown to have a 6b(*S*)-configuration in the 6,7-dihydrofoliamenthic acid moiety.

In view of the admixture of iridoids found in *Picconia excelsa*, this taxon is a typical member of the Oleaceae with typical oleoside derivatives and also with a content of verbascoside [4]. It is, however, specialized due to the presence of loganin and the loganin derivatives which are otherwise uncommon in the family.

EXPERIMENTAL

General procedures. Mps uncorr.; ^{1}H NMR (250 and 500 MHz): glucosides in D_2O or CD_3OD using the solvent peaks (4.75 or 3.31 ppm) as standards; acetates in $CDCl_3$ (7.27 ppm); ^{13}C NMR: solvent peak (δ 49.0) was used in CD_3OD, while C-6′ was set to 61.5 ppm as a standard [34] in D_2O; Prep. TLC: 20 × 40 cm plates coated with 1 mm layers of silicagel 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 (240 nm). Plant material of *Picconia excelsa* (Ait.) DC. was kindly supplied by Dr J. G. Luis, La Laguna, Tenerife. A voucher (36203) has been deposited at the Herbario de la Universidad de la Laguna and a duplicate in the Botanical Museum of Copenhagen (*legit.*: H. K. Leòn Arencibia & Mercedes Medina Pérez).

Work-up of plant material. Dried and powdered



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4 R = R' = H

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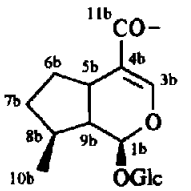

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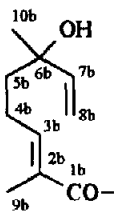

(Menthiafoloyl)

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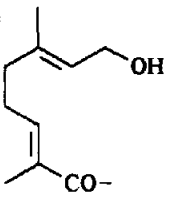

(Foliamenthoyl)

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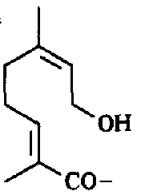

(6,(Z)-Foliamenthoyl)

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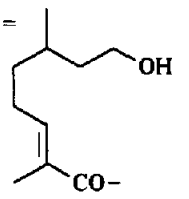


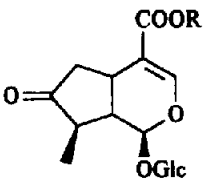
(6,7-Dihydrofoliamenthoyl)

foliage (118 g) of *P. excelsa* was homogenized with EtOH (400 ml) and the suspension was allowed to stand for 5 days. After removing insoluble material, the filtrate was evapd (20 g) and partitioned in H_2O–E_2O. The aq. layer was taken to dryness and the residue was dissolved in MeOH and passed through act. C (10 g). Concn of the filtrate gave a brownish foam (12.9 g), which was dissolved in H_2O (50 ml) and subsequently extracted with EtOAc (3 × 150 ml). Evapn afforded a water-soluble extract, **A** (7.8 g), and an EtOAc-soluble extract **B** (5.1 g).

Fractionation of extract (**A**). Chromatography was performed on a C-column (2 runs; 10:1 to 1:1) to give first a polar fraction **C** (0.33 g), followed by ketologanin (**2**, 0.56 g, 0.48%), loganin (**1**, 1.04 g, 0.88%), verbascoside (**10**, 0.6 g, 0.5%), crude oleoacteoside (**11**, 0.78 g), crude picconioside I (**12**, 0.89 g), and a late non-polar fraction eluted with MeOH (**D**, 0.29 g).

Rechromatography of fraction **C** (B-column; 6:1 to 2:1) gave three frs **C-1** (51 mg), **C-2** (60 mg), **C-3** (55 mg) and secoxyloganin (**6**, 21 mg, 0.018%). To **C-1** was added $NaHCO_3$ and rechromatography (B-column) gave a polar fraction **C-1a** (13 mg) followed by a fr. containing 6*β*-hydroxy-7-*epi*-loganin (**3**, 16 mg, 0.013%). Acidification (AcOH) of **C-1a** and rechromatography gave slightly impure 8-*epi*-kingisidic acid (**8**, 6 mg, 0.005%). Fraction **C-2** was treated like **C-1** and the polar part gave only ketologanic acid (**5**, 8 mg, 0.007%). Fr. **C-3** was treated similarly. Here, the polar part gave loganic acid (**4**, 16 mg, 0.01%) and a 4:1 mixt. (29 mg) of 8-*epi*-kingiside (**8**, 0.02%) and oleoside 11-methyl ester (**9**, 0.005%).

6β-Hydroxy-7-epi-loganin (**3**). Rechromatography of the fr. above gave pure **3** (4 mg) together with a less pure fr. (5 mg, 0.008%). Due to the small amount isolated, this compound was characterized solely by NMR. ^{1}H NMR (250 MHz, CD_3OD): δ 7.44 (*d*, J = 1.2 Hz, H-3), 5.40 (*d*, J = 4 Hz, H-1), 4.63 (*d*, J = 7.5 Hz, H-1′), 3.89 (*dd*, J = 2 and 12 Hz, H-6′), 3.73 (3H, *s*, OMe), 3.70 (2H, H-6 and H-6b′), 3.46 (*dd*, J = 6 and 8.5 Hz, H-7), 3.40-3.25 (3H, H-3′, H-4′, H-5′, obsc. by solvent signal), 3.16 (*dd*, J = 8 and



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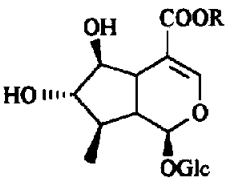

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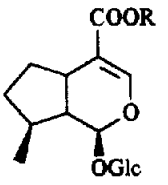

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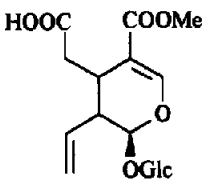

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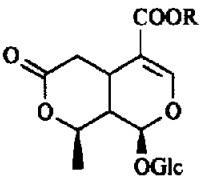

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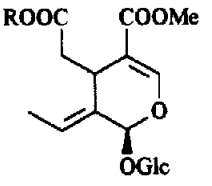

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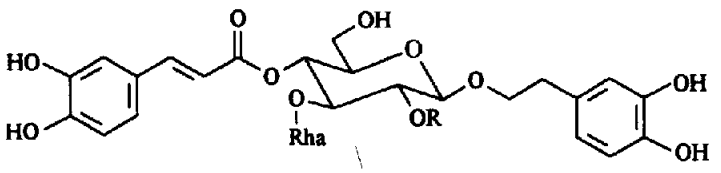

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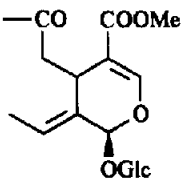
11 R = —CO COOMe



9 Hz, H-2′), 2.75 (*br ddd*, J = 1, 5 and 9 Hz, H-5), 2.03 (*dt*, J = 4 and 9 Hz, H-9), 1.70 (*m*, H-8), 1.16 (*d*, J = 6.5 Hz, 10-CH_3), virtually as reported [5], and ^{13}C NMR (63 MHz, CD_3OD): δ 17.2 (C-10), 39.4 (C-5), 41.1 (C-8), 44.4 (C-9), 51.9 (OMe), 84.3 (C-6*), 85.8 (C-7*), 96.4 (C-1), 111.2 (C-4), 153.0 (C-3), 170.0 (C-11), 100.1, 74.7, 78.0, 71.5, 78.3, and 62.7 (H-1′ to C-6′); * signals may be interchanged.

Ketologanic acid (**5**). $[\alpha]_D^{21}$ −107° (*c*, 1.2; MeOH); ^{1}H NMR (250 MHz, D_2O): δ 7.49 (*d*, J = 1 Hz, H-3), 5.64 (*d*, J = 2.5 Hz, H-1), 4.78 (*d*, J = 8 Hz, H-1′), 3.89 (*dd*, J = 2 and 12 Hz, H-6′), 3.67 (*dd*, J = 5.5 and 12 Hz, H-6′), 3.50-3.20 (5H, H-5, H-2′, H-3′, H-4′ and H-5′), 2.69 (*dd*, J = 8 and 20 Hz, H_a-6), 2.57 (*br d*, J = 20 Hz, H_b-6), 2.44 (*ddd*, J = 2.5, 7.5 and 11 Hz, H-9), 2.21 (*br dq*, J = 7 and 11 Hz, H-8), 1.09 (*d*, J = 7 Hz, 10-CH_3); ^{13}C NMR (63 MHz, D_2O): δ 215.9 (C-7), 171.4 (C-11), 153.3 (C-3), 110.7 (C-4), 95.4 (C-1), 45.3 (C-9), 44.5 (C-6), 42.9 (C-8), 27.1 (C-5), 13.0 (C-10), 99.4, 73.4, 76.4, 70.4, 77.2, and 61.5 (C-1′ through C-6′)—identical to a sample prepared by saponification of ketologanin (**2**) [4]. Found: C, 49.0; H, 6.4. $C_{16}H_{22}O_{10} \cdot H_2O$ requires: c, 49.0; H, 6.2%.

Oleoacteoside (**11**). According to NMR the fr. consisted mainly (~80%) of **11**. However, rechromatography did not improve the purity, so it was not further characterized. ^{1}H NMR (250 MHz, CD_3OD): essentially as reported [11]. ^{13}C NMR (63

MHz, CD_3OD): exactly as reported, except for a peak at δ 146.9 instead of the value assigned to C-4″ in the caffeoyl moiety (146.1) [11].

Picconioside I (**12**). The above crude **12** (0.89 g) was rechromatographed (B-column, 1:1). The residue containing **12** was dissolved in MeOH (50 ml) and filtered successively through act. C (0.2 g) and Al_2O_3 (4 g). Evapn of the filtrate afforded almost pure **12** (0.52 g; 0.4%) as a colourless syrup. Finally, prep. TLC ($CHCl_3$–MeOH 4:1) gave the pure compound (0.35 g; 0.3%) as a hygroscopic foam. $[\alpha]_D^{21} -74.3°$ (*c* 0.8; MeOH). ^1H NMR (500 MHz; CD_3OD): δ 7.43 (2H; *br s*, H-3a and H-3b), 5.29 (*d*, $J = 4.5$ Hz, H-1a), 5.23 (*d*, $J = 5.5$ Hz, H-1b), 5.19 (*br t*, $J = 4.5$ Hz, H-7a), 3.69 (3H, *s*, OMe), 3.11 (*br q*, $J = 8$ Hz, H-5a), 2.90 (*br q*, $J = 7.5$ Hz, H-5b), 2.30 (*ddd*, $J = 14.5$, 8 and 1 Hz, H_a-6a), 2.21 (*m*, H_a-6b), 2.15 (*m*, H-8a), 2.07 (*dt*, $J = 5$ and 9 Hz, H-9a), 1.98 (*br hept*, $J = 7$ Hz, H-8b), 1.89 (*m*, H_a-7b), *ca* 1.75 (2H; *m*s, H_b-6a and H-9b), 1.41 (*m*, H_b-6b), 1.21 (*br dq*, $J = 12$ and 8 Hz, H_b-7b), 1.09 (*d*, $J = 6.5$ Hz, 10a-Me), 0.96 (*d*, $J = 6.9$ Hz, 10b-Me); glucopyranosyl moieties: 4.68 and 4.66 (2H, *d*s, $J = 8$ Hz, 2 × H-1′), *ca* 3.90 (2H, *dd*s $J = 12$ Hz and 2 Hz, 2 × H_a-6′), 3.68 and 3.67 (2H, *dd*s, $J = 12$ and 6 Hz, 2 × H_b-6′), 3.40-3.18 (*m*, 8H, partly obsc. by the solvent signal, 2 × H-3′, 2 × H-5′, 2 × H-4′), 3.21 and 3.20 (2H, *dd*s, $J = 8$ and 9 Hz, 2 × H-2′). ^{13}C NMR: Table 1. Found C, 51.5; H, 6.9. $C_{33}H_{48}O_{18} \cdot 2H_2O$ requires: C, 51.6; H, 6.8%.

Alkaline hydrolysis of **12**. Picconioside I (**12**, 35 mg) was hydrolyzed in 0.5 M NaOH (6 ml) by heating at ~ 50° for 2 hr. The reaction mixt. was neutralized with 10% HOAc (pH 6). MPLC (B-column; 4:1 to 1:1) gave loganic acid (**4**, 9 mg) and deoxyloganic acid (**21**, 11 mg), identical to an authentic sample [4].

Acetylation of **12**. Acetylation (Py–Ac_2O, 1:1, 6 ml) of **12** (144 mg) gave an octaacetate (**12a**, 179 mg), which was recrystallized from EtOH, mp 115–117°; $[\alpha]_D^{21} -76°$ (*c* 1.0; $CHCl_3$). ^1H NMR (500 MHz; $CDCl_3$): loganin moiety: δ 7.28* (*br s*, H-3a), 5.21–5.19 (2H, obsc. by 2 × H-3′, H-7a and H-1a), 3.66 (*s*, 3H, 11a-OMe), 2.98 (*dt*, $J = 2 \times 8.5$ Hz and 5.5 Hz, H-5a), 2.21 (*ddd*, $J = 15$ Hz, 8.5 Hz and 1.0 Hz, H_a-6a), 2.17 (1H, obsc. by H_a-6a, H-9a), 1.94 (*m*, obsc. by AcO, H-8a), 1.82 (*dt*, $J = 15$ Hz and 2 × 5 Hz, H_b-6a), 1.01 (*d*, 3H, $J = 6.5$ Hz, 10a-Me); deoxyloganic acid moiety: 7.26* (*br s*, H-3), 5.12 (*d*, $J = 3.5$, H-1b), 2.83 (*q*, $J = 7.0$ Hz, H-5b), 2.13 (*ddd*, $J = 13$ Hz, 8.5 Hz and 4 Hz, H_a-6b), 1.81 (*m*, H_a-7b), 1.79 (*m*, H-8b), 1.75 (*dt*, $J = 2 \times 9.0$ Hz and 3.5 Hz, H-9b), 1.40 (*m*, H_b-6b), 1.18 (*m*, H_b-7b), 1.04 (*d*, 3H, $J = 5.5$ Hz, 10b-Me); glucopyranosyl moieties: 5.23-5.18 (*m*, 2H, obsc. by 2 × H-3′), 5.09 and 5.08 (*t*s, $J = 9.5$ Hz, 2 × H-4′), 4.97 (*m*, 2 × H-2′), 4.85 and 4.84 (*d*s, $J = 8$ Hz, 2 × H-1′), 4.29 and 4.27 (*dd*s, $J = 12.5$ and 5 Hz, 2 × H_a-6′), 4.12 (*dd*, 2H, $J = 12.5$ Hz and 2.5 Hz, 2 × H_b-6′), 3.72 (*m*, 2H, 2 × H-5′), 2.08, 2.07, 2.01, 2.00, 1.98, 1.97, 1.92 and 1.88 (*s*s, 8 × 3H, 8 × 3H, 8 × AcO); *signals may be interchanged. Found C, 54.4; H, 6.2. $C_{49}H_{64}O_{36} \cdot H_2O$ requires: C, 54.1; H, 6.1%.

Fractionation of the EtOAc extract. Extract **B** (5.1 g) together with fraction **D** from above was dissolved in MeOH (50 ml) and the soln filtered through act. C (1 g). Evapn gave a foam (3.45 g), which was chromatographed (C-column; 5:1 to 1:2). This gave first ketologanin (**2**, 140 mg, 0.12%) and loganin (**1**, 65 mg, 0.06%) followed by verbascoside (**10**, 300 mg, 0.25%), excelsioside (**13**, 150 mg, 0.13%), ligstroside (**14**, 350 mg, 0.30%) and impure picconioside I (**12**, 500 mg) was eluted with 1:1. Continued elution with 2:3 afforded a mixt. of picconiosides II–IV (fr. **F**, 0.80 g). Finally, elution with 1:2 gave impure picconioside V (**18**, 208 mg).

Fraction **F** was rechromatographed twice by prep. TLC (EtOAc–EtOH–toluene 4:1:1; each time with two developments) to give **15** (222 mg; R_f 0.66) and crude **16/17** (191 mg; R_f 0.63).

Picconioside II (**15**). Hygroscopic foam; $[\alpha]_D^{21} -29°$ (*c*, 1.5; MeOH); ^1H NMR (500 MHz; CD_3OD): δ 7.44 (*d*, $J = 1.2$ Hz, H-3), 5.31 (*d*, $J = 4.8$ Hz, H-1), 5.19 (*dt*, $J = 2 \times 5.0$ Hz and 1.3 Hz, H-7), 3.70 (*s*, 3H, 11-OMe), 3.12 (*br q*, $J = 8.0$ Hz, H-5), 2.29 (*ddd*, $J = 14.5$ Hz, 7.7 Hz and 1.5 Hz, H_a-6), 2.16 (*m*, H-8), 2.10 (*dt*, $J = 2 \times 8.8$ Hz and 4.8 Hz, H-9), 1.78 (*ddd*, $J = 14.5$ Hz, 7.7 Hz and 5.1 Hz, H_b-6), 1.07 (*d*, $J = 6.8$ Hz, 10-Me), 4.68 (*d*, $J = 8.0$ Hz, H-1′), 3.91 (*dd*, $J = 12.0$ Hz and 2.0 Hz, H_a-6′), 3.68 (*dd*, $J = 12.0$ Hz and 5.8 Hz, H_b-6′), 3.41-3.27 (*m*, 3H, obsc. by CD_2HOD-signal, H-3′, H-5′ and H-4′), 3.21 (*dd*, $J = 9.1$ Hz and 8.0 Hz, H-2′), 6.79 (*qt*, $J = 2 \times 7.8$ Hz and 3 × 1.4 Hz, H-3b), 5.93 (*dd*, $J = 17.3$ Hz and 10.8 Hz, H-7b), 5.24 (*dd*, $J = 17.3$ Hz and 1.6 Hz, H_{trans}-8b), 5.06 (*dd*, $J = 10.8$ Hz and 1.6 Hz, H_{cis}-8b), 2.35-2.20 (*m*, 2H, obsc. by H_a-6, 2 × H-4b), 1.84 (*s*, 3H, 9b-Me), 1.63 (*m*, 2H, 2 × H-5b), 1.28 (*s*, 3H, 10b-Me). ^{13}C NMR (62.5 MHz; CD_3OD): Table 1. Found C, 56.5; H, 7.5. $C_{27}H_{40}O_{12} \cdot H_2O$ requires: C, 56.4; H, 7.4%.

Picconioside III/IV *mixture* (**16/17**). Hygroscopic foam; ^1H NMR (500 MHz; CD_3OD): δ 7.43 (*t*-like), $J = 1.2$ Hz, 2 overlapping H-3s), 5.31 (*d*, $J = 4.9$ Hz, H-1 of Z), 5.30 (*d*, $J = 4.9$ Hz, H-1 of E), 5.19 (*br t*, $J = 4.4$ Hz, H-7), 3.70 (*s*, 3H, 11-OMe), 3.11 (*q*, $J = 8.0$ Hz, H-5), 2.30 (*dd*, $J = 14.7$ Hz and 7.9 Hz, H_a-6), 2.15 (*m*, H-8), 2.09 (*dt*, $J = 2 \times 8.8$ Hz and 4.9 Hz, H-9), 1.77 (*m*, obsc. by 9b-Me, H_b-6), 1.07 (*d*, $J = 6.8$ Hz, 10-Me), 4.76 (*d*, $J = 8.0$ Hz, H-1′), 3.91 (*dd*, $J = 12.0$ Hz and 2.0 Hz, H_a-6′), 3.68 (*dd*, $J = 12.0$ Hz and 6.0 Hz, H_b-6′), 3.39 (*t*, $J = 9.0$ Hz, H-3′), 3.36-3.27 (*m*, 2H, obsc. by CD_2HOD-signal, H-5′ and H-4′), 3.21 (*dd*, $J = 9.0$ Hz and 8.0 Hz, H-2′), 6.78 and 6.75 (*dt*s, $J = 2 \times 7.8$ Hz and 1.4 Hz, H-3b of *E*/*Z*), 5.43 (*br t*, $J = 6.7$ Hz, H-7b of *Z*), 5.43-5.38 (*m*, obsc. by H-7b of Z, H-7b of *E*), 4.11-4.05 (*d*s, 2H, $J = 6.7$ Hz, 2 × H-8b), 2.35 (*q*, 2H, $J = 7.8$ Hz, 2 × H-4b), 2.25 (*t*, 2H, $J = 7.5$ Hz, 2 × H-5b of Z), 2.18 (*q*, 2H, $J = 7.5$ Hz, 2 × H-5b of *E*), 1.85 (*br s*, 3H, 9b-Me), 1.77 (*br s*, 3H, 10b-Me of *Z*), 1.70 (*br s*, 3H, 10b-Me of *E*); *Z* and *E* above are configuration of the 6b,7b-double bond. ^{13}C NMR (62.5 MHz; CD_3OD): Table 1. Found

C, 56.5; H, 7.5. $C_{27}H_{40}O_{12}\cdot H_2O$ requires: C, 56.4; H, 7.4%.

Picconioside V (**18**). Rechromatography (B-column; 1:1 and 2:3) of the above impure picconioside V (208 mg) gave a syrup (146 mg), which was further purified by prep. TLC (EtOAc–EtOH–toluene 4:1:1) giving the pure compound (R_f 0.52; 88 mg; 0.07%) as a hygroscopic white foam. $[\alpha]_D^{21}-37°$ (*c*, 0.8; MeOH); ^{1}H NMR (500 MHz; CD_3OD): δ 7.43 (*d*, J = 1.2 Hz, H-3), 5.31 (*d*, J = 4.8 Hz, H-1), 5.19 (*dt*, $J = 2\times4.7$ Hz and 1.4 Hz, H-7), 3.70 (*s*, 3H, 11-OMe), 3.12 (*br q*, J = 8.0 Hz, H-5), 2.29 (*ddd*, J = 14.4 Hz, 7.7 Hz and 1.4 Hz, H_a-6), 2.16 (*m*, H-8), 2.09 (*dt*, $J = 2\times8.7$ Hz and 4.8 Hz, H-9), 1.78 (*ddd*, J = 14.4 Hz, 7.9 Hz and 5.2 Hz, H_b-6), 1.07 (*d*, 3H, J = 6.8 Hz, 10-Me), 4.67 (*d*, J = 8.0 Hz, H-1′), 3.91 (*dd*, J = 12.0 Hz and 2.1 Hz, H_a-6′), 3.68 (*dd*, J = 12.0 Hz and 6.0 Hz, H_b-6′), 3.41-3.27 (*m*, 3H, obsc. by the CD_2HOD-signal, H-3′, H-5′ and H-4′), 3.21 (*dd*, J = 9.2 Hz and 8.0 Hz, H-2′) 6.78 (*qt*, $J = 2\times7.5$ Hz and 3×1.4 Hz, H-3b), 3.65-3.55 (*m*, 2H, $2\times$H-8b), 2.23 (*q*, 2H, J = 8.0 Hz, $2\times$H-4b), 1.85 (*br s*, 9b-Me), 1.67-1.58 (*m*, 2H, H-6b and H_a-7b), 1.50 (*m*, H_a-5b), 1.39 (*m*, H_b-7b), 1.31 (*m*, H_b-5b), 0.95 (*d*, 3H, J = 6.7 Hz, 10b-Me). ^{13}C NMR (62.5 MHz; CD_3OD): Table 1. Found C, 54.6; H, 7.7. $C_{27}H_{42}O_{12}\cdot 2H_2O$ requires: C, 54.5; H, 7.8%.

Picconioside II *tetraacetate* (**15a**). Amorphous; $[\alpha]_D^{21}-40°$ (*c*, 0.7; $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.28 (*d*, J = 1.0 Hz, H-3), 5.24 (*d*, J = 2.5 Hz, H-1), 5.17 (*dt*, $J = 2\times5.0$ and 1.0 Hz, H-7), 3.71 (*s*, 3H, 11-OMe), 3.00 (*dt*, $J = 2\times9.2$ and 5.5 Hz, H-5), 2.30-2.17 (*m*, 2H, obsc. by $2\times$H-5″, H_a-6 and H-9), 2.00-1.90 (*m*, H-8), 1.83 (*dt*, J = 15.0 and 2×5.5 Hz, H_b-6), 1.02 (*d*, J = 6.8 Hz, 10-Me), 2.08, 2.01, 1.99 and 1.89 (*s*, each 3H, $4\times$Ac-Me); glc. signals: 5.21 (*t*, J = 9.8 Hz, H-3′), 5.08 (*t*, J = 9.8 Hz, H-4′), 4.98 (*dd*, J = 9.8 and 8.3 Hz, H-2′), 4.86 (*d*, J = 8.3 Hz, H-1′), 4.31 (*dd*, J = 12.5 and 4.7 Hz, H_a-6′), 4.13 (*dd*, J = 12.5 and 2.5 Hz, H_b-6′), 3.74 (*ddd*, J = 10.0, 4.7 and 2.5 Hz, H-5′); monoterpenoid part: 6.71 (*tq*, $J = 2\times7.8$ and 3×1.5 Hz, H-6″), 5.91 (*dd*, J = 17.4 and 10.8 Hz, H-2″), 5.23 (*dd*, J = 17.4 and 1.6 Hz, H_{trans}-1″), 5.08 (*dd*, J = 10.8 and 1.6 Hz, H_{cis}-1″), 2.30-2.17 (*m*, 2H, obsc. by H_a-6 and H-9, $2\times$H-5″), 1.80 (*s*, 3H, 9″-Me), 1.72-1.59 (*m*, 2H, $2\times$H-4″), 1.31 (*s*, 3H, 8″-Me). ^{13}C NMR (125 MHz; CD_3OD): Table 1. Found C, 57.7; H, 6.8. $C_{35}H_{48}O_{16}$ requires: C, 58.0; H, 6.7%.

Picconioside III/IV *pentaacetate mixture* (**16a/17a**). White needles, mp 97–99°, $[\alpha]_D^{21}-45°$ (*c*, 0.7; $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.30 (*br s*, H-3), 5.26 (*d*, J = 2.6 Hz, H-1), 5.20 (*br t*, J = 5.5 Hz, H-7), 3.70 (*s*, 3H, 11-OMe), 3.03 (*br q*, J = 8.0 Hz, H-5), 2.35-2.23 (*m*, H_a-6 and H-9), 1.98 (*m*, H-8), 1.90-1.83 (*m*, obsc. by Ac-Mes, H_b-6), 1.05 (*d*, J = 6.8 Hz, 10-Me), 2.10, 2.04, 2.01 and 1.92 ($4\times$Ac-Me), 5.24 (*t*, J = 9.7 Hz, H-3′), 5.11 (*t*, J = 9.8, H-4′), 5.00 (*dd*, J = 9.5 and 8.2 Hz, H-2′), 4.88 (*d*, J = 8.2 Hz, H-1′), 4.33 (*dd*, J = 12.5 and 4.5 Hz, H_a-6′), 4.15 (*dd*, J = 12.5 and 2.5 Hz, H_b-6′), 3.76 (*ddd*, J = 10.0, 4.5 and 2.5 Hz, H-5′), 6.71 (*br t*, J = 7.5 Hz, H-3b), 5.42 and 5.38 (*br ts*, J = 7.5 Hz, H-7b of Z:E 1:1), 4.60 and 4.57 (*ds*, J = 7.5 Hz, $2\times$H-8b), 2.35-2.23 (*m*, $2\times$H-5b), 2.25-2.23 and 2.18 (*ts*, J = 7.5 Hz, $2\times$H-4b of Z:E 1:1), 2.06 and 2.05 (*ss*, Ac-Me), 1.84 (*s*, 3H, 9b-Me), 1.80 and 1.74 (*ss*, 10b-Me); Z and E are the configuration of the 6b,7b-double bond. ^{13}C NMR (125 MHz; CD_3OD): Table 1. Found C, 57.6; H, 6.6. $C_{37}H_{50}O_{17}$ requires: C, 58.0; H, 6.6%.

Picconioside V *pentaacetate* (**18a**). Amorphous; $[\alpha]_D^{21}-47°$ (*c*, 0.9; $CHCl_3$); ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.29 (*d*, J = 1.0 Hz, H-3), 5.25 (*d*, J = 2.7 Hz, H-1), 5.18 (*dt*, $J = 2\times5.0$ and 1.0 Hz, H-7), 3.68 (*s*, 3H, 11-OMe), 3.02 (*dt*, $J = 2\times9.0$ and 5.0 Hz, H-5), 2.31-2.23 (*m*, 2H, H_a-6 and H-9), 2.05-1.90 (*m*, obsc. by Ac-Mes, H-8), 1.85 (*dt*, J = 15.2 and 2×5.2 Hz, H_b-6), 2.09, 2.04, 2.03, 2.00 and 1.90 (*s*, each 3H, $5\times$Ac-Me), 5.22 (*t*, J = 9.5 Hz, H-3′), 5.09 (*t*, J = 9.8 Hz, H-4′), 4.99 (*dd*, J = 9.5 and 8.1 Hz, H-2′), 4.86 (*d*, J = 8.1 Hz, H-1′), 4.32 (*dd*, J = 12.3 and 4.5 Hz, H_a-6′), 4.14 (*dd*, J = 12.3 and 2.4 Hz, H_b-6′), 3.75 (*ddd*, J = 10.0, 4.5 and 2.4 Hz, H-5′), 6.70 (*tq*, $J = 2\times7.7$ and 3×1.5 Hz, H-3b), 4.14-4.06 (*m*, 2H, $2\times$H-8b), 2.22-2.12 (*m*, 2H, $2\times$H-4b), 1.82 (*s*, 3H, 9b-Me), 1.70 (*m*, H_a-7b), 1.58 (*m*, H-6b), 1.52-1.42 (*m*, 2H, H_b-7b and H-5b), 1.32 (*m*, H_b-5b), 0.95 (*d*, 3H, J = 6.9 Hz, 10b-Me). ^{13}C NMR (125 MHz; CD_3OD): Table 1. Found C, 57.8; H, 6.9. C_{37}, $H_{50}O_{17}$ requires: C, 57.8; H, 6.8%.

Synthesis of 7-O-*acetyl loganin* (**20**). Loganin (**1**, 65 mg) was acetylated with Py–Ac_2O (1:1; 1 ml; 2 hr at RT). Work-up was followed by methanolysis (NaOMe in MeOH; pH 9) for 30 min. After addition of HOAc till pH 6, the mixt. was chromatographed on a B-column. Elution with 3:2 gave **20** (61 mg); amorphous; $[\alpha]_D^{21}-65°$ (*c*, 0.5; MeOH); ^{1}H NMR (250 MHz; CD_3OD): δ 7.47 (*d*, J = 1 Hz, H-3), 5.31 (*d*, J = 5.0 Hz, H-1), 5.20 (*br dt*, J = 1.5 and 5 Hz, H-7), 3.74 (*s*, 3H, 11-OMe), 3.13 (*br q*, J = 8 Hz, H-5), 2.31 (*ddd*, J = 14.5, 7.5 and 1.5 Hz, H_a-6), 2.15 (*m*, H-8), 2.07 (*dt*, J = 5 and 9.5 Hz, H-9), 1.78 (*ddd*, J = 14.5, 8 and 5 Hz, H_b-6), 1.10 (*d*, 3H, J = 6.5 Hz, 10-Me), 4.70 (*d*, J = 8 Hz, H-1′), 3.94 (*dd*, J = 12 and 2 Hz, H_a-6′), 3.70 (*dd*, J = 12 and 6 Hz, H_b-6′), 3.42 (*t*, J = 9 Hz, H-3′), *ca* 3.35 (2H obsc. by the solvent signal, H-4′ and H-5′), 3.23 (*dd*, J = 9 and 8 Hz, H-2′). ^{13}C NMR (62.5 MHz; CD_3OD): Table 1. Found C, 51.1; H, 6.5. $C_{37}H_{50}O_{17}$ requires: C, 50.7; H, 6.7%.

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