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IRIDOID GLUCOSIDES IN FOUQUIERIACEAE

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Key Word Index—*Fouquieria* sp; Fouquieriaceae; iridoid glucosides; iridoid glucoside 10-acetates; galioside; splendoside; 6β-hydroxysplendoside; 7β-hydroxysplendoside; 6β, 7β-epoxysplendoside; adoxoside; adoxosidic acid; 6β-hydroxyloganin; loganin.

Abstract—From three *Fouquieria* sp. 12 iridoid glucosides were isolated and identified. Eight of these were structurally related to galioside (monotropein methylester), while four were hydroxy substitution products of deoxyloganin. In three cases the glucoside occurred together with the corresponding 10-*O*-acetate.

INTRODUCTION

Recently the presence of iridoid glucosides in Fouquieriaceae [1] was confirmed [2] and structures for some of these iridoids were proposed. The affinities of the family were discussed in the light of chemical evidence and an alternative systematic position near Ericales and Cornales was suggested [2]. Here we present details of the isolation and characterization of twelve iridoids from three species of Fouquieriaceae.

RESULTS AND DISCUSSION

Fouquieriaceae is a small family of trees and shrubs, some of them succulent, growing in arid parts of Mexico and S.W. United States. The only genus *Fouquieria* has been divided into three subgenera (Table 1) [3], of which representatives of the subgenera *Fouquieria* and *Idria* have been examined here. Each of the three species contained several iridoid glucosides (Table 1). The substances from both species of the subgenus *Fouquieria* were structurally related to galioside (monotropein methylester, **1**), differing from this only in the nature of the substituents at C-6 and C-7. Determination of the configuration at C-8 was possible by ^{13}C NMR spectroscopy: galioside (**1**) and gardenoside (**17**) are C-8 epimers; it has been shown that the chemical shift of C-9 may be used to distinguish between C-8 epimers of this structural type [4, 5, 12]. For **1** and **17** were reported the values 45.4 and 52.4 ppm, respectively, recorded in CD_3OD [4]. In D_2O (glucosides) and $CDCl_3$ (acetates) we find a mean of 44.8 ± 1.7 ppm for C-9 in compounds **1–16**, except for the epoxides **8** (42.7 ppm) and **14** (39.4 ppm). For **17–20** with 8-β-OH (gardenoside) configuration we find 50.7 ± 0.7 ppm. Thus, all 8, 10-dioxygenated glucosides in *Fouquieria* (**1**, **2**, **4**, **5**, **7**, **9**, **10** and **12**) have the 8-α-OH-configuration.

F. digueti. Galioside (monotropein methylester, **1**) is known as a constituent of *Galium mollugo* [6]. Monotropein itself has been found in *G. verum* [7], but otherwise occurs mainly within Ericales. Splendoside (6, 7-dihydromonotropein methylester, **4**) is a new natural compound, but has previously been prepared by catalytic hydrogenation of monotropein methylester [8]. 6β, 7β-Epoxysplendoside (**7**) was purified as the penta-acetate **8**. That **8** contained an epoxide function was evident from the chemical shifts (59.0 and 58.2 ppm) and coupling constants ($^1J_{CH}$ = 192 and 188 Hz) of two of the carbon atoms [9]. Analysis of the ^1H NMR spectrum showed that the epoxide function was in positions 6 and 7. From biosynthetic considerations (analogy with **9** and **12**) the configuration was presumed to be β. Attempts to synthesize the β-epoxide acetate by reaction of **3** with *m*-chloroperbenzoic acid were unsuccessful. However, the corresponding α-epoxide acetate could be synthesized by stereoselective oxidation of **3** with *tert*-butyl hydroperoxide, catalysed by vanadyl acetylacetonate [10]. The product **14** was not identical with the naturally derived epoxide acetate, which therefore must have the structure **8**.

A fraction from the CC of the original glycoside mixture consisted of two compounds in the proportion 5:1. According to the ^1H NMR spectrum the major compound was 6-hydroxysplendoside, as H-6

Table 1. Distribution of iridoid glucosides in *Fouquieria* sp.

Sub-genus		**1**	**2**	**4**	**5**	**7**	**9**	**10**	**12**	**21**	**23**	**24**	**26**
Fouquieria	*F. diguetii*	+	+	+	+	+	+	+	+				
Fouquieria	*F. splendens*	+		+			+		+	+			
Idria	*F. columnaris*										+	+	+

(*m*, δ 4.34) was coupled to H-5 (*dd*, δ 2.94), H-7x (*ddd*, δ 1.98), and H-7y (*ddd*, δ 1.89). The β-configuration was assigned to 6-hydroxysplendoside for two reasons: (1) an analysis [11] of the possible conformers of the 6β- and 6α-isomers, based on the ^{1}H NMR coupling constants, gave the preferred conformations V_8 and $^7T_8$ for 6β-hydroxysplendoside (**9**), while a reasonable agreement could not be reached for the 6α-isomer (**10**) in any conformation; (2) according to a new method of predicting ^{13}C NMR spectra it is possible to distinguish between isomers, enantiomerically substituted at one position [12]. The ^{13}C NMR spectrum of **11** (β), reduced to the set of shift values from the aglucone part, S(**11**β) (Table 2), may be regarded as the spectrum of **6**, S(**6**), modified by a set of increments E(6β-OAc), the latter representing the effect of substitution of a 6β-OAc group, and calculated as E(6β-OAc) = S(**29**) − S(**31**). Thus S(**11**β) = S(**6**) + E(6β-OAc); the deviation from the real spectrum is designated Δ_β = *S*(**11**β) − S(**11**). In the same way, E(6α-OAc), S(**11**α) and Δ_α can be calculated. Comparison shows that the Δ_β values for C-1, C-3, and C-4 are much smaller than the corresponding Δ_α values, while only minor divergencies are seen for the remaining carbon atoms. Structure **11**(β) must be preferred, in agreement with the results above. The same conclusion has been reached using a different approach [12].

The minor component, 7β-hydroxysplendoside (**12**), was purified as the hexa-acetate **13**. That **13** was 7-substituted followed from the ^{1}H NMR spectrum: by decoupling a signal at δ 5.00 a multiplet at δ 2.25 collapsed to a double doublet, which consequently must arise from one of the H-6 protons. The other H-6 signal, concealed by the acetyl signals, could be seen by a partial relaxation experiment, at *ca* δ 2.0. The remaining question of the configuration was solved by synthesis of 7α-hydroxysplendoside penta-acetate (**16**). Application of the Woodward reaction [13] to geniposide penta-acetate (**15**) would be expected to give a product with an OH- and an OAc-group *cis* to each other and on the α-face of the molecule. The product obtained was **16** with an 8α-OH (C-9 = 43.2 ppm) and a 7α-OAc group (H-7 = 4.96 ppm). **16** was different from **13**, which consequently must be 7β-hydroxysplendoside penta-acetate.

Besides **1**, **4**, and **9** small amounts of the corresponding 10-monoacetates **2**, **5** and **10** were isolated. Their structure were proved by ^{1}H NMR (AcO: 2.1–2.2 ppm, 10-Hs showing the expected acetylation shift), and ^{13}C NMR (downfield shift of C-10: *ca* 3.0, C-7: *ca* 0.3, and C-9: *ca* 0.8 ppm; upfield shift of C-8: *ca* 1.8 ppm).

F. splendens. Adoxoside (**21**) was identified by comparison of the penta-acetate **22** with an authentic sample [14].

F. columnaris. Adoxosidic acid (**23**) (a novel iridoid) was converted to **22** by methylation (CH_2N_2) and acetylation. A less polar fraction was separated into loganin (**26**) and a new iridoid glucoside, 6β-hydroxyloganin (**24**). In the ^{1}H NMR spectrum of **24** signals from H-1, H-5, H-8, H-9, -OCH_3 and CH_3-10 could be identified. By partial relaxation the signals of H-6 and H-7 appeared as triplets (δ 3.89 and 3.96) with *J*s = *ca* 5 Hz. **24** gave a hexa-acetate corresponding to the gross structure **25**, disregarding stereochemistry. The 6- and 7-OH groups are *cis*, because reaction of **24** with acetone–$CuSO_4$ readily

Table 2. Calculation of ^{13}C NMR spectra of **11**α and **11**β

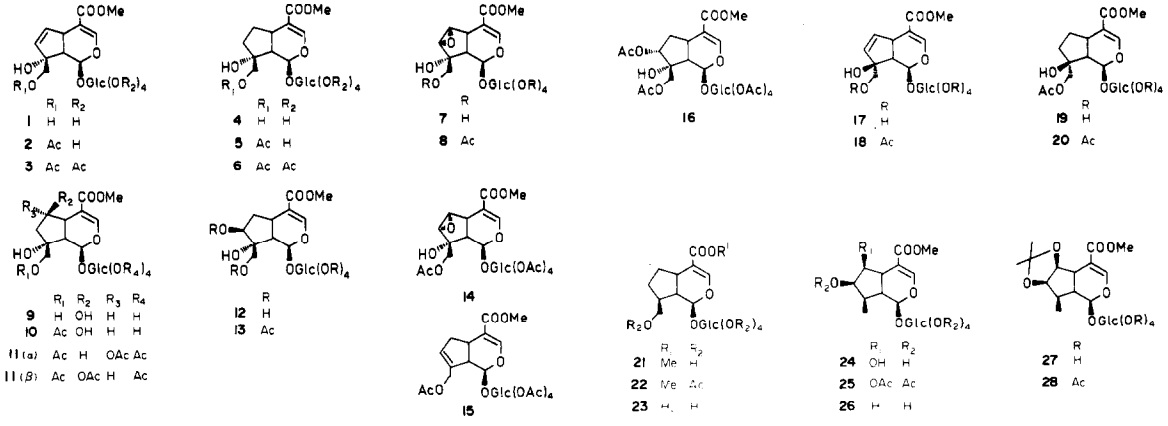
	S(**29**)	S(**31**)	E(6β–OAc)	S(**6**)	S(**11**β)	S(**11**)	$\Delta\beta$
C-1*	93.9	95.1	−1.2	96.5	95.3	93.7	+1.6
C-3	150.8	149.2	+1.6	151.0	152.6	151.8	+0.8
C-4	108.8	112.9	−4.1	111.5	107.4	108.1	−0.7
C-5	38.6	32.3	+6.3	35.3	41.6	38.0	+3.6
C-6	78.3	30.8	+47.5	30.9	78.4	76.8	+1.6
C-7	39.3	32.7	+6.6	36.9	43.5	42.4	+1.1
C-8	32.7	34.6	−1.9	80.5	78.6	78.3	+0.3
C-9	46.6	47.9	−1.3	45.3	44.0	44.0	0
C-10	20	19.3	+0.7	70.6	71.3	71.1	+0.2
C-11	166.5	167.2	−0.7	167.2	166.5	166.3	+0.2
	S(**30**)	S(**31**)	E(6α-OAc)	S(**6**)	S(**11**α)	S(**11**)	$\Delta\alpha$
C-1	98.4	95.1	+3.3	96.5	99.8	93.7	+6.1
C-3	152.5	149.2	+3,3	151.0	154.3	151.8	+2.5
C-4	106.5	112.9	−3.0	111.5	105.1	108.1	−3.0
C-5	39.1	32.3	+6.8	35.3	42.1	38.0	+4.1
C-6	76.7	30.8	+45.9	30.9	76.8	76.8	0
C-7	39.7	32.7	+7.0	36.9	43.9	42.4	+1.5
C-8	33.8	34.6	−0.8	80.5	79.7	78.3	+1.4
C-9	45.5	47.9	−1.1	45.3	42.9	44.0	−1.1
C-10	20	19.3	+0.7	70.6	71.3	71.1	+0.2
C-11	167.5	167.2	+0.3	167.2	167.5	166.3	+1.2

E(6β-OAc) = S(**28**) ÷ S(**30**); E(6α-OAc) = S(**29**) ÷ S(**30**); $\Delta\beta$ = S(**11**β) ÷ S(**11**); $\Delta\alpha$ = S(**11**α) ÷ S(**11**).

*Shift values in ppm.

Table 3. ^{1}H NMR data of some 6, 7-isopropylidene derivatives

	H-5 $J_{5,6}$	H-6 $J_{6,7}$	H-7 $J_{7,8}$	H-8 $J_{8,9}$	H-9 $J_{5,9}$	$J_{1,9}$
28	2.87	4.58	4.40	1.7	2.36	
	0	5.5	6.0	12.0	7.5	2.0
32 [14]		4.56	4.33	2.48	2.92	
		5.0	<1.0	7.5		1.9
33 [14]		4.63	4.45	1.57	2.30	
		5.4	5.4	12.6		1.4
34 [15]						
	<1	5.0	6.0	12.0	7.3	2.0



yielded an isopropylidene derivative (**27**). In the acetate **28** $J_{5,6} \sim 0$ Hz; this is only compatible with a 6β, 7β-substitution. To determine the configuration at C-8 a comparison was made between **28** and the corresponding derivatives of pulchelloside I (**32**), and II (**33**) [15] (Table 3).

Since $J_{1,9}$ in **28**, **32** and **33** is ~2.0 Hz the conformation of the six-membered ring in these compounds is the same. There is perfect agreement between the data for **28** and for the pulchelloside II derivative **33**, both regarding the coupling constants, especially $J_{8,9}$ ($\geqq$12 Hz), and the chemical shifts of H-8 and H-9, while the corresponding values for **32** are very different from those of **28** and **33**. This strongly suggests a β-configuration for the methyl group at C-8.

According to our method of using ^{13}C NMR data [12], the chemical shift of C-9 can be calculated from a base value to which an increment for each substituent on the cyclopentane ring is added. The base value is different for an α- and a β-methyl group at C-8:

		24(8-α-Me) (ppm)	**24**(8-β-Me) (ppm)
Calculation of δ C-9 in **24**:	base value	43.5	48.3
	6β-OH subst.	−1.7	−1.7
	7β-OH subst.	−2.0	−2.0
		39.8	44.6

The observed value is 44.7 ppm, strongly supporting the β-configuration at C-8, in agreement with ^{1}H NMR data.

Proton coupling constants of *bis*-isopropylidene nyctanthoside triacetate (**34**) are included in Table 3.

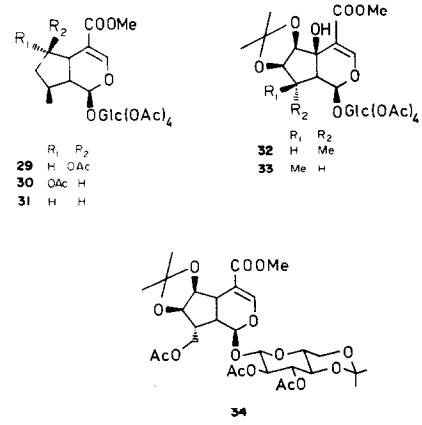


Table 4. ^{13}C NMR data of iridoids in *Fouquieria* (22.7 or 67.9 MHz)

	1	2	3	4	5	6	8	9	10	11
C-1	95.0(173)	95.0	94.2(176)	96.0(173)	95.5	98.2(171)	92.3(176)	95.1(173)	94.8	93.6(173)
C-3	151.9(193)	151.9	150.0(194)	153.0(193)	152.6	150.8(191)	151.6(193)	153.6(193)	153.5	151.7(191)
C-4	111.0	110.8	110.9	112.2	112.6	111.3	106.8	109.8	109.3	108.0
C-5	37.7(136)	37.6	37.8(139)	33.6(136)	32.4	35.2(132)	31.6(140)	40.4(139)	40.2	37.7(138)
C-6	132.7(165)	131.8	131.8(167)	30.6(130)	30.1	30.7(132)	59.0(192)*	76.3(138)	75.9	76.7(145)
C-7	137.9(168)	138.3	137.7(170)	36.0(133)	36.3	36.7(132)	58.3(188)*	44.0(128)	44.2	42.3(129)
C-8	85.5	83.8	83.4	82.9	80.9	80.4	77.6	81.7	80.0	78.3
C-9	44.7(129)	45.7	45.1(131)	45.7(134)	46.6	45.1(130)	42.7(135)	44.5(130)	45.2	43.9(132)
C-10	67.1(139)	70.7	69.5(148)	68.6(142)	71.0	70.2	68.1(148)	69.0(142)	72.0	70.8(145)
C-11	170.2	170.0	166.6	170.4	170.6		166.1	170.4		166.2
OMe	52.6	52.6	51.4	52.6	52.5	51.2	51.2	52.7	52.6	51.3
C-1′	99.0(161)	99.0	96.3(163)	99.8(162)	99.4	96.3(162)	95.0(162)	99.2(160)	99.0	96.1(162)
C-2′	73.3	73.4	70.7	73.5	73.4	70.4	70.3	73.4	73.3	70.3
C-3′	76.3	76.4	72.4	76.5	76.3	72.1	72.1	76.3	76.3	72.1
C-4′	70.3	70.3	68.3	70.3	70.2	68.0	67.8	70.3	70.2	67.8
C-5′	76.9	76.9	72.4	77.1	77.0	72.1	72.1	77.0	77.0	72.1
C-6′	61.4	61.4	61.8	61.5	61.4	61.4	61.4	61.4	61.4	61.4

	13	14	16	18	19	20	24	25	28
C-1	94.1(173)	98.6(176)	93.1(173)	92.1(177)	95.1(173)	93.5(171)	97.4(172)	94.0(170)	93.8
C-3	150(192)	152.5(193)	149.6(192)	148.9(195)	152.3(195)	150.0(194)	153.1(192)	150.6(190)	150.5
C-4	111.4	104.5	112.2	110.8	112.3	112.4	111.3	109.9	109.6
C-5	29.7(138)	36.4(134)	27.5(137)	36.9(138)	32.3(136)	31.9*d*	38.4(140x)	35.5(130)*	38.5*
C-6	35.9(132)	60.0(190)*	34.9(134)	133.5(168)*	29.3(132x)	28.9 *t*	79.5(143)	76.8(145)*	83.0*
C-7	80.2(151)	56.1(192)*	74.8(145x)	134.9(172)*	34.1(131)	34.8*t*	75.1(149)	74.6*	81.6*
C-8	80.6	79.3	78.1	83.1	83.5	80.8	37.9(130)	35.1(139)*	37.6*
C-9	44.4(128)	39.4(135)	43.2(132)	50.5(134)	50.3(130)	50.0(134)	44.7(134)	44.5(137)	42.7
C-10	66.3(147)	67.3	66.5(146)	67.6(148)	65.9(142)	67.9(150x)	13.4(124)	13.1	11.6
C-11	166.5	166.6		166.1		167.0	170.8	166.2	
OMe		51.4	51.1	51.0	52.5	51.2	52.8	51.3	51.3
C-1′	96.6(161)	99.2(164)	96.1(162)	95.1(165)	99.2(161)	96.0(165)	99.4(161)	95.7(160)	95.4
C-2′	70.2	70.8	70.3	70.3	73.3	70.6	73.5	70.4	70.3
C-3′	72.0	72.4	72.0	71.9	76.3	72.2	76.5	72.1	72.0
C-4′	67.9	68.2	67.9	67.8	70.2	68.2	70.4	68.0	67.9
C-5′	72.0	72.4	72.0	72.2	77.0	72.5	77.2	72.2	72.3
C-6′	61.4	61.4	61.4	61.4	61.4	61.4	61.6	61.5	61.5

*Not assigned with certainty.

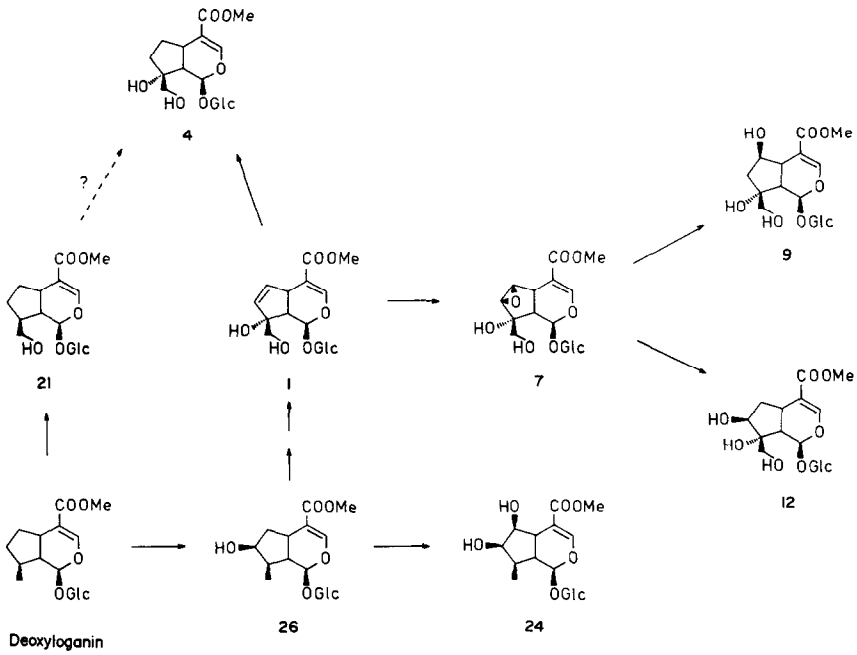


Fig. 1. Hypothetical biosynthesis of *Fouquieria* iridoids.

The configuration at C-8 in nyctanthoside has been determined as α by the conformational analysis of **34** [16]. However, the J values of **34** are almost identical with those of **28** and **33**, which implies that the configuration at C-8 should be reversed. A $^7T_8$ or a V_8 conformation, somewhat strained because of steric compression, would account for the observed coupling constants in **28** and **34**, except for $J_{8,9} = 12.0$ Hz, which is above the maximum value attainable by the Carplus equation (cf. Ref. [15]).

If one accepts that the biosynthesis of monotropein, and presumably galioside (**1**), proceeds from loganin via geniposide [17], then one may imagine the biosynthesis of the *Fouquieria* iridoids proceeds as shown in Fig. 1. Galioside (**1**) is epoxidized to **7**, which can be reduced to either **9** or **12**. Reduction of the double bond in **1** leads to splendoside (**4**). Alternatively, **4** may arise by 8-hydroxylation of adoxoside (**21**), but, apparently, adoxoside is not metabolized to other iridoids in any of the species in which it occurs. It is often found together with loganin (**26**) and secoiridoids [14, 18], and presumably arises, parallel to loganin, by hydroxylation of deoxyloganin, although this remains to be demonstrated. 6β-Hydroxyloganin (**24**) is very likely generated by hydroxylation of loganin.

EXPERIMENTAL

Microanalyses were performed at Novo Microanalytical Laboratory, Bagsvaerd, Denmark. ^{1}H NMR: 90 MHz, unless otherwise indicated, free glucosides in D_2O, acetates in $CDCl_3$. Fresh plant material (*F. diguetii* and *F. columnaris*) obtained from the Botanical Garden in Copenhagen was kept at −23°. *F. diguetii* was identified by Dr. K. Rahn, The Botanical Garden, Copenhagen. The identity of *F. columnaris* could not be verified owing to lack of flowering material, and a voucher (IOK-52-75) is deposited in the Botanical Museum, Copenhagen. *F. splendens* was collected in western Texas and identified by Professor T. Mabry.

F. diguetii. Leaves and twigs (150 g) were treated as described [19, 20], giving a mixture of glycosides (0.720 g). Repeated CC (Merck: Si gel, 0.040–0.063 mm) and prep. TLC yielded the following compounds, in order of increasing polarity: *splendoside* 10-*acetate* (**5**, 19 mg, 0.01%), ^{1}H NMR: δ 4.11 (*s*, 2H-10), 2.12 (*s*, OAc); acetylation gave splendoside penta-acetate, **6** (see below); *galioside* 10-*acetate* (**2**, 34 mg, 0.02%), $[\alpha]_D^{21} - 63.6°$ (MeOH; *c* 0.3), ^{1}H NMR: δ 4.25 (*s*, 2H-10), 2.17 (*s*, OAc); acetylation gave galioside penta-acetate (**3**) (see below); 6-β-*hydroxysplendoside* 10-*acetate* (**10**, 30 mg, 0.02%), ^{1}H NMR: δ 4.25 [*s*(*br*), 2H-10], 2.19 (*s*, OAc); acetylation gave the hexa-acetate **11** (see below); *splendoside* (**4**, 45 mg, 0.03%), ^{1}H NMR: δ 7.52 (*d*, $J_{3,5}$ = 1.5 Hz, H-3), 5.54 (*d*, $J_{1,9}$ = 4.0 Hz, H-1), 3.76 (*s*, OMe), 3.60 (*s*, 2H-10), *ca* 3.0 (*m*, H-5), 2.34 (*dd*, $J_{1,9}$ = 4.0 Hz, $J_{5,9}$ = 9.0 Hz, H-9), characterized as the penta-acetate **6**, mp 124–125°, (lit. [8] 122–124°), $[\alpha]_D^{21} - 68.5°$ (EtOH; *c* 0.7), (lit. [8] − 69.2°, EtOH), ^{1}H NMR: δ 7.39 (*d*, $J_{3,5}$ = 1.5 Hz, H-3), 5.23 (*d*, $J_{1,9}$ = 6.5 Hz, H-1), 4.07 (AB-syst., 2H-10), 3.71 (*s*, OMe), *ca* 2.8 (*m*, H-5), *ca* 2.1 (H-9), 1.98–2.04 (5 × OAc); *galioside* (**1**, 136 mg, 0.09%), identified as the penta-acetate **3**, mp 149–150° (lit. [6] 150–151°), $[\alpha]_D^{21} - 101.8°$ (Me_2CO; *c* 0.6), (lit. [6] − 103.2°, Me_2CO), ^{1}H NMR as reported [6]; 6β,7β-*epoxysplendoside* (**7**, 17 mg, 0.01%), ^{1}H NMR: δ 7.53 (*d*, $J_{3,5}$ = 1.5 Hz, H-3), 5.66 [*s*(*br*), H-1], 4.00 [*d*(*br*), $J_{6,7}$ = 2.5 Hz, H-6], 3.76 (*s*, OMe), 3.48 (*d*, $J_{6,7}$ = 2.5 Hz, H-7), 2.22 [*d*(*br*), $J_{5,9}$ = 8.5 Hz, H-9]; purified as the penta-acetate **8**, mp 182–183° (EtOH), $[\alpha]_D^{22} - 85.6°$ ($CHCl_3$; *c* 0.5), ^{1}H NMR (270 MHz): δ 7.46 (*d*, $J_{3,5}$ = 1.5 Hz, H-3), 5.57 [*s*(*br*), H-1], 4.26 (AB-syst., 2H-10), 3.98 [*d*(*br*), $J_{6,7}$ = 2.5 Hz, H-6], 3.76 (*s*, OMe), 3.31 [*d*(*br*), $J_{6,7}$ = 2.5 Hz, H-7], 3.22 [*d*(*br*), $J_{5,9}$ = 8.5 Hz, H-5], 2.33 [*d*(*br*), $J_{5,9}$ = 8.5 Hz, H-9], 1.87–2.11 (5 × OAc). (Found: C, 50.6; H, 5.4; $C_{27}H_{34}O_{17}$. $\frac{1}{2}H_2O$ requires: C, 50.7; H, 5.5%.) 6-β-*hydroxysplendoside* (**9**, 50 mg, 0.03%) as a *ca* 5:1 mixt. with 7-β-*hydroxysplendoside* (**12**); ^{1}H NMR

(270 MHz); δ 7.54 (*d*, $J_{3,5}$ = 1.5 Hz, H-3), 5.63 (*d*, $J_{1,9}$ = 2.5 Hz, H-1), 4.34 (*m*, H-6), 3.76 (*s*, OMe), 3.67 (*s*, 2H-10), 2.94 [*dd*(*br*), $J_{5,6}$ = 3.0 Hz, $J_{5,9}$ = 9.0 Hz, H-5], 2.65 (*dd*, $J_{1,9}$ = 2.5 Hz, $J_{5,9}$ = 9.0 Hz, H-9). Separation was achieved after acetylation, yielding: (1) 6-β-hydroxysplendoside hexacetate (**11**), mp 140–141°, $[\alpha]_D^{23}$ − 80.5° ($CHCl_3$; *c* 0.9), ^{1}H NMR: δ 7.47 (*d*, $J_{3,5}$ = 1.5 Hz, H-3), 5.51 (*d*, $J_{1,9}$ = 3.5 Hz, H-1), 5.37 (*m*, H-6), 4.11 (*s*, 2H-10), 3.74 (*s*, OMe), 2.98 (*m*, $J_{3,5}$ = 1.5 Hz, $J_{5,6}$ = 3.5 Hz, $J_{5,9}$ = 8.5 Hz, H-5), 2.60 (*dd*, $J_{1,9}$ = 3.5 Hz, $J_{5,9}$ = 8.5 Hz, H-9), 1.87–2.20 (6 × OAc), (Found: C, 51.3; H, 5.7; $C_{29}H_{38}O_{18}$ requires: C, 51.6; H, 5.7.); (2) 7-β-Hydroxysplendoside hexa-acetate (**13**), mp 131–133°, $[\alpha]_D^{23}$ − 57.0° ($CHCl_3$; *c* 0.5). ^{1}H NMR (270 MHz): δ 7.40 (*d*, $J_{3,5}$ = 1.5 Hz, H-3), 5.38 (*d*, $J_{1,9}$ = 4.5 Hz, H-1), 5.00 (*t*, $J_{6x,7}$ = 4.5 Hz, $J_{6y,7}$ = 4.5 Hz, H-7), 4.18 (AB-syst., 2H-10), 3.71 (*s*, OMe), 3.05 (*m*, H-5), 2.45 (*dd*, $J_{1,9}$ = 4.5 Hz, $J_{5,9}$ = 9.5 Hz, H-9), 2.25 (*ddd*, $J_{5,6x}$ = 7.5 Hz, $J_{6x,6y}$ = 14.0 Hz, $J_{6x,7}$ = 4.5 Hz, H-6*x*), 2.10 (*ddd*, $J_{5,6y}$ = 7.5 Hz, $J_{6x,6y}$ = 14.0 Hz, $J_{6y,7}$ = 4.5 Hz, H-6y), 1.96–2.09 (6 × OAc). (Found: C, 51.4, H, 5.6; $C_{29}H_{38}O_{18}$ requires: C, 51.6; H, 5.7.)

6α, 7α-*Epoxysplendoside penta-acetate* (**14**) [10]. A soln of **3** (40 mg, 0.065 mmol) in C_6H_6 (2 ml) was heated to reflux. Vanadyl acetylacetonate [21] (2 mg) and *tert*-butylhydroperoxide [22] (10 μl = *ca* 0.07 mmol 70% TBHP) were added, the initial dark red colour changing during 0.5 hr to yellow-green. After two additions more of TBHP the product was separated by TLC, yielding **14** (syrup, 15 mg), $[\alpha]_D^{22}$ − 6.5° ($CHCl_3$; *c* 0.9), ^{1}H NMR: δ 7.47 (*d*, $J_{3,5}$ = 2.0 Hz, H-3), 5.31 (*d*, $J_{1,9}$ = 9.0 Hz, H-1), 4.11 (AB-syst., 2H-10), *ca* 3.8 (H-6, hidden by OMe), 3.76 (*s*, OMe), 3, 49 (*d*, $J_{6,7}$ = 3.0 Hz, H-7), 3.09 (*m*, $J_{5,9}$ = 9.0 Hz, H-5), 1.93 (*t*, $J_{1,9}$ = 9.0 Hz, $J_{5,9}$ = 9.0 Hz, H-9), 1.98–2.14 (5 × OAc). (Found: C, 50.8; H, 5.8; $C_{27}H_{34}O_{17}$. $\frac{1}{2}H_2O$ requires: C, 50.7; H, 5.5.)

7α-*Hydroxysplendoside hexa-acetate* (**16**) [13]. Geniposide penta-acetate (**15**, 120 mg, 0.2 mmol) and AgOAc (70 mg, 0.44 mmol) in HOAc (1.5 ml) was stirred while pulverized I_2 (53 mg, 0.21 mmol) was added during 0.25 hr. After 1.5 hr H_2O–HOAc (1:25, 0.1 ml) was added and the mixture heated to 95–100° for 1.5 hr, the colour changing to dark brown. NaCl (50 mg) in H_2O (0.5 ml) was added and the mixture stirred 0.3 hr and worked up, yielding unreacted **15** (45 mg) and **16** (30 mg), mp 175–176°, $[\alpha]_D^{23}$ − 99.2° ($CHCl_3$; *c* 0.2), ^{1}H NMR (270 MHz): δ 7.37 [*s*(*br*), H-3], 5.51 (*d*, $J_{1,9}$ = 3.5 Hz, H-1), 4.96 (*dd*, $J_{6x,7}$ = 7.0 Hz, $J_{6y,7}$ = 9.0 Hz, H-7), 4.08 (AB-syst., 2H-10), 3.71 (*s*, OMe), 2.90 (*q*-like H-5), 2.64 (*dt*, $J_{5,6x}$ = 8.0 Hz, $J_{6x,6y}$ = 13.0 Hz, $J_{6x,7}$ = 7.0 Hz, H-6*x*), 2.38 (*dd*, $J_{1,9}$ = 3.5 Hz, $J_{5,9}$ = 10.0 Hz, H-9), 1.91–2.11 (6 × OAc), 1.73 (*dt*, $J_{5,6y}$ = 7.5 Hz, $J_{6x,6y}$ = 13.0 Hz, $J_{6y,7}$ = 9.0 Hz, H-6y). (Found: C, 51.4; H, 5.6; $C_{29}H_{38}O_{18}$ requires: C, 51.6; H, 5.7.)

F. splendens. From dry leaves were isolated **1** (0.2%), **4** (0.08%), **9** (0.04%) and **12** (0.03%). In the bark was further found adoxoside (**21**) (0.1%), identified as the penta-acetate **22** (mp, NMR) [14].

F. columnaris. Leaves and twigs (500 g), treated as usual, yielded by Me_2CO-elution from Si gel: A (1.6 g), and by elution with Me_2CO–MeOH (1:1) B (3.8 g). From A were isolated 6β-hydroxyloganin (**24**) and loganin (**26**) by rev. phase chrom. (Merck Lichroprep RP-8, H_2O–MeOH, 3:1): (**24**) (250 mg, 0.05%), mp 220–222° (EtOH, H_2O), $[\alpha]_D^{21}$ − 107.2° (MeOH; *c* 0.4), ^{1}H NMR (270 MHz): δ 7.48 [*s*(*br*), H-3], 5.38 (*d*, $J_{1,9}$ = 3.6 Hz, H-1), 3.96 and 3.89 (*ts*, *Js* = *ca* 5 Hz, H-6 and H-7), 3.74 (*s*, OMe), 2.89 [*dd*(*br*), $J_{5,6}$ = 5.4 Hz, $J_{5,9}$ = 9.0 Hz, H-5], 2.26 (*dt*, $J_{1,9}$ = 3.6 Hz, $J_{5,9}$ = 9.0 Hz, $J_{8,9}$ = 9.6 Hz, H-9), 1.96 (*m*, $J_{7,8}$ = 5.1 Hz, $J_{8,9}$ = 9.6 Hz, $J_{8,10}$ = 6.5 Hz, H-8), 1.09 (*d*, $J_{8,10}$ = 6.5 Hz, 3H-10). (Found: C, 50.3; H, 6.5; $C_{17}H_{26}O_{11}$ requires: C, 50.2; H, 6.5.) Acetylation gave the hexa-acetate **25**, mp 130–131.5°, $[\alpha]_D^{21}$ − 91.4° ($CHCl_3$; *c* 0.3), ^{1}H NMR: δ 7.33 (*d*, $J_{3,5}$ = 1.5 Hz, H-3), 5.26 (*d*, $J_{1,9}$ = 2.5 Hz, H-1), 3.66 (*s*, OMe), 2.90 (*m*, H-5), 2.44 (*dt*, $J_{1,9}$ = 2.5 Hz, $J_{5,9}$ = 9.0 Hz, $J_{8,9}$ = 9.0 Hz, H-9), 1.89–2.11 (6 × OAc), 1.05 (*d*, $J_{8,10}$ = 6.5 Hz, 3H-10). (Found: C, 52.1; H, 5.9; $C_{29}H_{38}O_{17}$. $\frac{1}{2}H_2O$ requires: C 52.2; H, 5.9) Loganin (**26**, 90 mg, 0.02%, mp, NMR). From B was likewise isolated adoxosidic acid (**23**, 160 mg, 0.03%), identified (mmp, NMR), after reaction with CH_2N_2 and acetylation, as adoxoside penta-acetate (**22**) [14].

6,7-O-*Isopropylidene-6*β-*hydroxyloganin tetra-acetate* (**28**). **24** (50 mg) and $CuSO_4$ (150 mg) were refluxed 2 hr in dry Me_2CO (50 ml). Rev. phase chrom. (H_2O–MeOH, 2:1) gave **27** (30 mg), which was converted to the tetra-acetate **28** (17 mg), mp 154–156° (EtOH), $[\alpha]_D^{21}$ − 115.6° ($CHCl_3$; *c* 0.3); ^{1}H NMR: δ 7.30 (*d*, $J_{3,5}$ = 1.5 Hz, H-3), 5.36 (*d*, $J_{1,9}$ = 2.0 Hz, H-1), 4.58 (*d*, $J_{6,7}$ = 5.5 Hz, H-6), 4.40 (*dd*, $J_{6,7}$ = 5.5 Hz, $J_{7,8}$ = 6.0 Hz, H-7) 3.74 (*s*, OMe), 2.87 (*dd*, $J_{3,5}$ = 1.5 Hz, $J_{5,9}$ = 7.5 Hz, H-5), 2.36 (*m*, $J_{1,9}$ = 2.0 Hz, $J_{5,9}$ = 7.5 Hz, $J_{8,9}$ = 12.0 Hz, H-9), 1.87–2.07 (4 × OAc), *ca* 1.7 (*m*, H-8), 1.29 and 1.47 (*ss*, isoprop.-Me), 1.11 (*d*, $J_{8,10}$ = 6.5 Hz, 3H-10). (Found: C, 54.4; H, 6.1; $C_{28}H_{38}O_{15}$ requires: C, 54.7; H, 6.2.) Gardenoside (**17**) was isolated from *Gardenia jasminoides*, and dihydrogardenoside (**19**) prepared from gardenoside by catalytic hydrogenation (Pd–H_2) [23].

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