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IRIDOID GLUCOSIDES IN *GRISELINIA*, *ARALIDIUM* AND *TORICELLIA*

SØREN ROSENDAL JENSEN and BENT JUHL NIELSEN

Department of Organic Chemistry, The Technical University of Denmark, 2800 Lyngby, Denmark

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Key Word Index—*Griselinia*; *Aralidium*; *Toricellia*; Cornales: iridoid glucosides; griselinoside; aralidioside; coumarin glucoside; magnolioside; syringoside; ^{13}C NMR data.

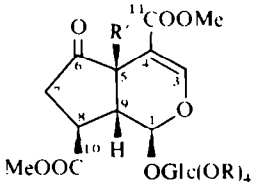
Abstract—From three of five investigated species of *Griselinia*, a new iridoid glucoside, griselinoside, was isolated. It was found to be present also in foliage of *Aralidium pinnatifidum* and *Toricellia angulata*, accompanied in the former by aralidioside, another novel iridoid glucoside. The structures and absolute configurations of the two iridoids were elucidated by NMR spectroscopy and chemical conversions. From *G. littoralis* and *T. angulata* the glucosides magnolioside and syringoside, respectively, were isolated. ^{13}C NMR spectra are given for thirteen iridoid derivatives.

INTRODUCTION

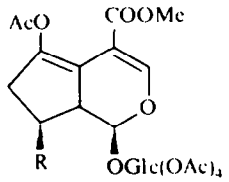
In continuation of our studies on iridoids and other glycosides in the genus *Cornus* [1] and, more broadly, Cornaceae and its allies [2], we present the results of studies on *Griselinia* Forst. f., *Aralidium* Miq., and *Toricellia* DC. All three genera have formerly been included in the Cornaceae proper at one time or another, but are now segregated into monogeneric families [3, 4] with six, one and three species, respectively. The systematic position of *Aralidium* has recently been subjected to a multi-disciplinary investigation concluding its relationship to Cornaceae and its allies (cf. [3]). The present paper gives the chemical details of our part [5] of that work.

RESULTS

Griselinia. In *G. littoralis* Raoul, *G. lucida* Forst. and *G. ruscifolia* (Clos) Taub. a new iridoid, griselinoside, was found. Its structure, **1**, was deduced by NMR spectroscopy. Thus, in the ^{1}H NMR spectrum of **1**, two methoxycarbonyl groups could be observed, whereas the spectrum of the tetraacetate (**2**) exhibited a broad doublet (H-5) at unusually low field (δ 3.56), indicating the presence of an oxo group at C-6. The ^{13}C NMR spectrum confirmed the presence of these functionalities and was in accord with structure **1**. The structure and absolute configuration of all centres in griselinoside were proved by hydrogenation with Pt/H_2 in acetic acid to give forsythide dimethyl ester (**15**) of known absolute configuration [6].



1 R = R′ = H
2 R = Ac; R′ = H
6 R = H; R′ = OH
7 R = Ac, R′ = OH
8 R = Ac; R′ = OAc



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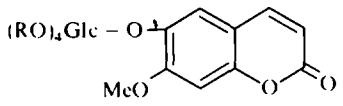
11 R = Me



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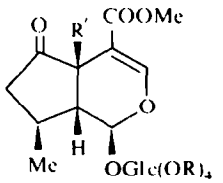
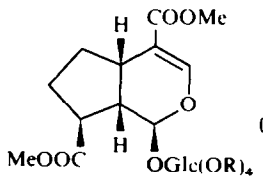
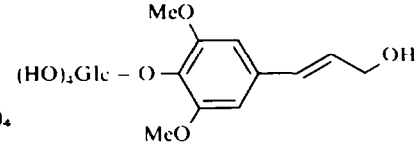
5 R = Ac



9 R = R′ = H
10 R = Ac; R′ = H
12 R = H; R′ = OH
13 R = Ac; R′ = OH
14 R = Ac, R′ = OAc



15 R = H
16 R = Ac



17

Upon acetylation in pyridine–acetic anhydride, **1** gave two acetates: the expected tetraacetate (**2**) and a pentaacetate of the 5,6-enol form (**3**). The structure of **3** was established by NMR and UV as well as its conversion into the tetraacetate (**2**) by the treatment with *p*-toluenesulfonic acid in methanol. Acetylation of **1** in ethyl acetate with perchloric acid as a catalyst yielded **3** as the main product. In addition to **1**, magnolioside (**4**) [7] was isolated from *G. littoralis*. Its identity was ascertained by NMR and comparison of the acetate (**5**) with an authentic sample prepared by methylation [8] and acetylation of aesculin.

No iridoids could be detected in *G. alata* Ball or *G. jodinifolia* (Griseb.) Taub.

Aralidium pinnatifidum (leaves or bark) contained griselinoside (**1**), accompanied by another iridoid glucoside, aralidioside (**6**), as a minor component. The ^{1}H NMR spectrum of **6** revealed the presence of two methoxycarbonyl groups, and the signal from H-3 (7.91, *s*) indicated the presence of a hydroxy group at C-5. The ^{13}C NMR spectrum was similar to that of **1**, showing the same functionalities, apart from a singlet at 74.0 at the expense of a doublet at high field in **1**. Again, the low-field position (157.5 vs 154.6 in **1**) of the signal assigned to C-3, was in keeping with a 5-OH substituent. Acetylation of **6** gave rise to a tetraacetate (**7**), and, on prolonged reaction, to a pentaacetate (**8**), all in accord with the proposed structure. Conversion of **3** to **8** could be achieved by oxidation with *m*-chloroperbenzoic acid in chloroform, presumably by epoxidation of the 5,6-double bond, followed by rearrangement [9]. The reaction was slow (1–2 days), and the epoxide could not be detected in the reaction mixture. Therefore, identical configurations for **1** and **6** at all centres except C-5 was proved.

Acetylation of cornin (**9**) in the presence of an acid catalyst as in the preparation of **3** provided the 5,6-enol pentaacetate (**11**). Treatment of **11** with MCPB as above gave hastatoside pentaacetate (**14**), identical with **14** prepared from hastatoside (**12**). This analogy, together with the almost complete correspondence of the ^{13}C NMR data for **6**, **7** and **8** with those of **12**, **13** and **14**, respectively (Table 1) points to the same absolute stereochemistry (5β-hydroxy) for aralidioside and hastatoside [10].

Toricellia angulata Oliv. var. *intermedia* (Harms) Hu contained griselinoside (**1**) and trace amounts of aralidioside (**6**). Another constituent, the phenolic glucoside, syringoside (**17**), was identified by its physical data [11].

Griselinoside (**1**) is a constituent also of some species of *Verbena* [12, 13].

EXPERIMENTAL

General procedures were as earlier described [8, 14]. ^{1}H NMR spectra were run at 90 MHz (glucosides: D_2O–DSS; acetates: $CDCl_3$–TMS).

Griselinia littoralis. Dry powdered leaf material (100 g) was extracted with EtOAc for 5 hr in a Soxhlet. The extract was evapd, H_2O (100 ml) was added, and the suspension extracted with $CHCl_3$ (100 ml) and Et_2O (2 × 200 ml). The conc aq. soln was eluted with H_2O (500 ml) from a column of Al_2O_3 (neutral, 50 g) yielding a residue (1.42 g) of crude glycosides. Upon addition of a few ml of H_2O, magnolioside (**4**, 60 mg) crystallized; mp 223–225° (loss of H_2O at *ca* 145°) (lit. [7]: mp 227°). Tetraacetate (**5**), mp 174.5–176° (lit. [7]: 176°); mmp with specimen prepared by successive methylation [8] and acetylation of aesculin showed no depression; ^{1}H NMR: δ 7.59 (*d*, J = 9.5 Hz, H-4), 7.25 (*s*, H-5), 6.83 (*s*, H-8), 6.30 (*d*, J = 9.5 Hz, H-3), 3.91 (*s*, OMe), 2.13–2.05 (4 × OAc). Chromatography of the mother liquid from above (Si gel; $CHCl_3$–MeOH, 8:1 to 4:1) gave griselinoside (**1**, 480 mg) and a mixture of **1** and **4**. Further separation on Sephadex G-15 yielded **4** (33 mg, total 0.09%) and **1** (180 mg, total 0.7%). Passage through act. carbon gave an analytical specimen of **1** as a foam, $[\alpha]_D^{21}$ – 117° (*c* 0.3; MeOH); $\lambda_{max}^{M.OH}$ nm (log ε): 235 (4.0); ^{1}H NMR: δ 7.66 (*br. s*, H-3), 5.36 (*d*, $J_{1,9}$ = 7.0 Hz, H-1), 4.87 (*d*, H-1′), 3.80 and 3.78 (*s*, 2 × OMe), 3.6 (H-5), 2.96 (*m*, H-9). (Found: C, 47.57; H, 5.76. $C_{18}H_{24}O_{12}$; H_2O requires: C, 48.00; H, 5.82%).

Acetylation (Py–Ac_2O, 20°) of **1** (740 mg) for 18 hr gave rise to a mixture (850 mg) from which **2** (390 mg) could be crystallized, mp (EtOH) 188.5–189°; $[\alpha]_D^{21}$ – 122° (*c* 0.3; $CHCl_3$); λ_{max}^{MeOH} nm (log ε): 233 (3.97); ^{1}H NMR: δ 7.46 (*d*, $J_{3,5}$ = 1, 5 Hz, H-3), 5.09 (*d*, $J_{1,9}$ = 6.5 Hz, H-1), 3.81 and 3.78 (*s*, 2 × OMe), 3.56 (*br. d*, $J_{5,9}$ = 8.0 Hz, H-5), *ca* 2.8 (*m*, H-9), 2.12–2.00 (4 × OAc). (Found: C, 51.96; H, 5.31. $C_{26}H_{32}O_{16}$ requires: C, 52.00; H, 5.37%). Prep. TLC (Et_2O) of the mother liquid gave griselinoside 5,6-enol pentaacetate (**3**, 80 mg), mp (EtOH) 174–176°; $[\alpha]_D^{24}$ 9.4 (*c* 0.6, $CHCl_3$); $\lambda_{max}^{M.OH}$ nm (log ε): 211 (4.05), 267 (4.08); ^{1}H NMR: δ 7.45 (*br. s*, H-3), 5.20 (*d*, $J_{1,9}$ = 8 Hz, H-1), 3.78 and 3.75 (*s*, 2 × OMe), 2.19–2.04 (4 × OAc). (Found: C, 52.36; H, 5.46. $C_{28}H_{34}O_{17}$ requires: C, 52.17; H, 5.63%).

Hydrogenation of griselinoside (**1**, 760 mg) was performed in HOAc (50 ml) with Pt (160 mg) as the catalyst, for 2 hr. The product mixture was separated into 3 fractions: A (99 mg, C-6 epimeric alcohols), B (97 mg, **1**) and C (295 mg, forsythide dimethyl ester, **15**). Acetylation of **15** (61 mg) gave **16** (52 mg), mp (EtOH) 146–148°; (lit. [6]: mp 143–144°); ^{1}H NMR: δ 7.36 (*d*, $J_{3,5}$ = 1.5 Hz, H-3), 5.26 (*d*, $J_{1,9}$ = 3 Hz, H-1), 3.71 (*s*, 2×OMe) 2.9 (*m*, H-5), 2.6 (*m*, H-9), 2.11–1.91 (4 × OAc). (Found: C, 53.13; H, 5.86. Calc. for $C_{26}H_{34}O_{15}$: C, 53.24; H, 5.84%). Identical with an authentic sample (mp, mmp, ^{1}H NMR). Dry foliage of *G. lucida* (13 g) and *G. ruscifolia* (24 g) were extracted as above to give 25 mg (0.2%) and 74 mg (0.3%) of **1**, respectively.

Aralidium pinnatifidum. Ground, dry leaves (48 g) were extracted as above to give 1.7 g of crude glycosides. Chromatography (Si gel; $CHCl_3$–MeOH, 3:1) yielded **1** (750 mg, 1.5%) and a mixture (143 mg) from which aralidioside (**6**, 100 mg, 0.2%) was isolated as a foam, $[\alpha]_D^{24}$ – 211° (*c* 0.3; MeOH); $\lambda_{max}^{M.OH}$ nm (log ε): 232 (3.99); ^{1}H NMR: δ 7.91 (*s*, H-3), 6.11 (*br. s*, H-1), 3.80 and 3.72 (*s*, 2 × OMe).

Acetylation of **6** for 2 hr gave the tetraacetate **7**, mp 134–135°, $[\alpha]_D^{23}$ – 198° (*c* 0.4; MeOH); λ_{max}^{MeOH} nm (log ε): 228 (3.91); ^{1}H NMR: δ 7.63 (*s*, H-3), 5.87 (*d*, $J_{1,9}$ = 1.0 Hz, H-1), 3.96 (5-OH), 3.80 and 3.74 (*s*, 2 × OMe), 3.0–2.7 (4H, H-7, 8, 9), 2.11–1.96 (4 × OAc). (Found: C, 50.64; H, 5.33. $C_{26}H_{32}O_{17}$ requires: C, 50.66, H, 5.23%). Acetylation for 2 days provided the pentaacetate **8**, mp 188–190°; $[\alpha]_D^{25}$ – 232° (*c* 0.5, MeOH); λ_{max}^{MeOH} nm (log ε): 231 (3.96); ^{1}H NMR: δ 7.74 (*s*, H-3), 5.89 (*d*, $J_{1,9}$ = 1.0 Hz, H-1), 3.80 and 3.74 (*s*, 2 × OMe), 3.1–2.5 (4H, H-7, 8, 9), 2.13–1.96 (4 × OAc). (Found: C, 51.10; H, 5.22. $C_{28}H_{34}O_{18}$ requires: C, 51.06; H, 5.20%).

Oxidation of **3** (221 mg) was performed in $CHCl_3$ (2 ml) with MCPB (66 mg, 1.1 eq) for 2 days. Washing with $NaHCO_3$ soln followed by prep. TLC (Et_2O) gave **8** (138 mg) as the sole product. This sample was indistinguishable from **8** prepared by acetylation of **6**. Bark of *A. pinnatifidum* contained 0.8% of **1** and 0.2% of **6**.

Toricellia angulata foliage (dry, 62 g) was extracted as above to give 0.31 g of crude glycosides. Prep. TLC gave **1** (140 mg, 0.2%) and trace amounts of **6** and **17**. From 42 g of twigs were extracted 0.56 g crude glycosides, yielding 320 mg **1** (0.7%), a trace of **6**, and

Table 1. ^{13}C NMR spectral data for iridoids and acetates (22.6 MHz)*

	C-1	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	OMe	C-1′
1	96.9 *d*(170)	154.6 *d*(195)	104.0 *s*	44.0 *d*(138)	215.5 *s*	37.9 *t*(134)	39.8 *d*(134)	40.7 *d*(141)	176.3 *s*	169.2 *s*	53.9 52.9	100.3 *d*(163)
2	95.5 *d*(168)	151.7 *d*(194)	104.8 *s*	43.2 *d*(138)	209.3 *s*	37.4 *t*(132)	38.8 *d*(137)	40.2 *d*(141)	173.5 *s*	166.1 *s*	52.6 51.7	97.2 *d*(164)
3	101.4	153.9	105.4	110.9	141.0	41.6	36.7	46.2	173.0	164.5	52.1 51.5	96.4
6	95.3 *d*(178)	157.5 *d*(195)	105.4 *s*	74.0 *s*	212.0 *s*	—†	36.2 *d*(136)	47.1 *d*(139)	175.4 *s*	167.9 *s*	53.9 52.8	100.2 *d*(162)
7	93.8 *d*(177)	153.2 *d*(192)	107.6 *s*	73.0 *s*	206.8 *s*	34.8 *t*(135)	35.9 *d*(135)	47.2 *d*(138)	172.3 *s*	165.5 *s*	52.8 51.9	96.3 *d*(163)
8	92.7 *d*(180)	154.9 *d*(195)	103.3 *s*	76.8 *s*	201.3 *s*	36.1 *t*(135)	36.6 *d*(131)	43.9 *d*(140)	171.8 *s*	164.2 *s*	52.8 51.7	95.3 *d*(163)
9	96.8 *d*(172)	154.2 *d*(194)	104.5 *s*	43.3 *d*(137)	219.7 *s*	43.7 *t*(131)	29.5 *d*(135)	44.9 *d*(139)	19.8 *q*(127)	169.5 *s*	52.9	99.8 *d*(162)
10	94.8 *d*(169)	150.8 *d*(194)	105.1 *s*	43.0 *d*(139)	212.0 *s*	43.0 *t*(131)	28.6 *d*(133)	44.3 *d*(134)	19.8 *q*(129)	166.2 *s*	51.4	96.4 *d*(164)
11	102.9 *d*(171)	153.9 *d*(193)	105.7 *s*	111.8 *s*	143.3 *s*	40.7 *t*(131)	33.7 *d*(130)	49.7 *d*(137)	19.8 *q*(125)	165.4 *s*	51.5	97.0 *d*(164)
12	95.0 *d*(177)	157.0 *d*(196)	105.6 *s*	74.4 *s*	215.4 *s*	40.7 *t*(131)	26.3 *d*(132)	52.1 *d*(133)	19.4 *q*(126)	168.2 *s*	52.7	100.1 *d*(162)
13	93.0 *d*(174)	152.4 *d*(192)	107.8 *s*	72.9 *s*	209.4 *s*	40.3	25.7 *d*(131)	51.8	19.7 *q*(129)	165.6 *s*	51.5	95.8 *d*(161)
14	92.2 *d*(176)	154.3 *d*(194)	103.7 *s*	77.2 *s*	204.0 *s*	41.8 *t*(131)	27.1 *d*	48.4 *d*(135)	19.1 *q*(127)	164.6 *s*	51.6	95.2 *d*(162)
16	94.7	150.3	112.0	33.0	30.6	27.6	44.5	44.3	175.1	167.5	52.0 51.2	96.0

*Spectra of glucosides were recorded in D_2O (dioxane), and those of acetates in $CDCl_3$ (TMS) essentially as earlier reported [14]; the signals arising from the glucosyl moieties had a pattern as expected [14].

†Signal not recorded due to D_2O exchange.

40 mg (0.1%) of **17**: mp (EtOH) 184.5–186°, lit. [11] 189°; $[\alpha]_D^{21}$ − 24° (*c* 0.4, H_2O), lit. [11] − 18.5°; ^1H NMR: δ 6.85 (2H, *s*, arom. H), 6.7–6.2 (2H, AB-part of ABX_2-syst.), 5.02 (gluc. H-1), 4.25 (2H, X_2-part of ABX_2-syst.), 3.86 (*s*, 2 × OMe).

Cornin-5,6-enol pentaacetate (**11**) was prepared by treatment of cornin tetraacetate (**10**, 180 mg) in EtOAc with Ac_2O and a catalytic amount of $HClO_4$ for 2 hr, followed by work-up and prep. TLC to give **11** (129 mg) as an unstable syrup, $[\alpha]_D^{21}$ − 23° (*c* 0.5; MeOH); λ_{max}^{MeOH} nm(log ε): 214 (4.01), 269 (4.02); ^1H NMR: δ 7.40 (*s*, H-3), 5.20 (*d*, $J_{1,9}$ = 2.5 Hz, H-1), 3.74 (*s*, OMe), 2.16–2.02 (4 × OAc), 1.22 (*d*, $J_{8,10}$ = 7 Hz, 10-CH_3). (Found: C, 53.70; H, 5.70. $C_{27}H_{34}O_{15}$ requires: C, 54.18; H, 5.72%).

Oxidation of **11** (60 mg) essentially as for **3** gave hastatoside pentaacetate (**14**, 27 mg) as a syrup, identical with a sample prepared by acetylation (Py–Ac_2O, 4 days) of hastatoside (**12**) isolated from *Verbena hastata* [10]. $[\alpha]_D^{24}$ − 216° (*c* 1.2, MeOH); λ_{max}^{MeOH} nm(log ε): 229 (3.8). (Found: C, 53.17; H, 5.94. $C_{27}H_{34}O_{16}$ requires: C, 52.77; H, 5.57%). ^1H NMR: δ 7.65 (*s*, H-3), 5.67 (*d*, $J_{1,9}$ = 1.5 Hz, H-1), 3.74 (*s*, OMe), 3.11 (*dd*, $J_{1,9}$ = 1.5, $J_{8,9}$ = 11 Hz, H-9), 2.12–1.96 (4 × OAc), 1.24 (*d*, $J_{8,10}$ = 7 Hz, 10-Me).

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