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# IRIDOIDS FROM *VIBURNUM BETULIFOLIUM*

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**Key Word Index**—*Viburnum betulifolium*; Caprifoliaceae; iridoid glucoside; acylated iridoid alloside; viburnalloside; decapetaloside.

**Abstract**—Two iridoid glycosides have been isolated from *Viburnum betulifolium*. Viburnalloside, the major leaf glycoside, is composed of an iridoid aglucone acylated at C-1 with isovaleric acid and with a di-*O*-acetyl-β-D-allopyranosyl moiety attached through a glycosidic bond to C-11. Decapetaloside (10-hydroxyiridodial glucoside) has been isolated from the bark. The structure and absolute configuration of viburnalloside have been established by spectroscopic means, and those of decapetaloside by chemical correlation with adoxoside.

## INTRODUCTION

*Viburnum betulifolium* Batal. is a deciduous shrub native to Central and Western China [1]; apparently, nothing is known about its chemistry. Iridoids have been reported, however, from several other species of *Viburnum* [2–7].

## RESULTS AND DISCUSSION

Leaves and bark of the plant were examined separately. Preliminary experiments showed the leaf extract to be unstable in contact with silica gel. $^1$H NMR spectroscopy of the crude aqueous extract revealed the presence of a single major constituent, but after silica gel chromatography the spectrum of the main fraction became more complex. Consequently, an extract was prepared avoiding contact with silica gel and alumina. Chromatography of this extract on Sephadex G 15 gave viburnalloside (**1**) as a colourless syrup. Its $^1$H NMR spectrum was very similar to those of the 'opulus iridoids' [4], except that only one isovaleroyl and two acetyl moieties were present. Acetylation gave a penta-acetate (**1a**) demonstrating the presence of three unhindered hydroxyl groups. The $^{13}$C NMR spectrum of **1** exhibited the signals expected from the three acyl groups and six signals ascribable to a 2,3-di-*O*-acyl-β-allopyranosyl moiety, as seen on comparing it with the spectrum of opulus iridoid I (**2**, Table 1). The remaining ten signals were assigned to an iridoid aglucone resembling **2** but without the secondary acetoxyl group, suggesting the overall structure **1**. The changes seen in the $^{13}$C NMR shift values when comparing the spectra of **1** and **1a** on one hand, and those of **1a** and **2a**, on the other, were also consistent with the proposed structure (Table 1). In order to establish the stereochemistry and positions of the acyl groups, **1a** was cleaved with boron trifluoride etherate, followed by acetylation, giving penta-*O*-acetyl-β-D-allopyranose and the di-acetate (**3**) of the cyclized aglucone. This experiment established the following: (a) the nature of the sugar moiety; (b) the relative stereochemistry at C-5, C-8 and C-9; and (c) the position of the isovaleroyl group, since we had shown earlier that boron trifluoride etherate affects only acyl groups at acetalic centres [4]. Furthermore, the specific rotation of **3** (+41°) was the same as that found for **4**, derived from opulus iridoid I (**2**) [4], suggesting the same absolute stereochemistry for these two compounds as that of valerosidatum [8].

Another compound (**5**) was isolated as the main glucoside from an extract of bark from twigs and branches of *V. betulifolium*. Its NMR spectra were in accord with

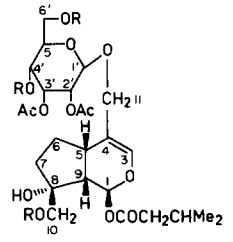
Table 1. $^{13}$C NMR spectral data of compounds **1**, **1a**, **2** and **2a** (22.6 MHz, $CDCl_3$).

| C | **1*** ($D_2O$) | **1a*** | **2**† | **2a**† |
|---|---|---|---|---|
| 1 | 91.4 | 89.9 | 89.5 | 89.4 |
| 3 | 140.7 | 140.3 | 139.9 | 140.2 |
| 4 | 114.6 | 113.2 | 113.3 | 113.0 |
| 5 | 34.0 | 35.4 | 31.9 | 32.0 |
| 6 | 28.2 | 28.5 | 34.8 | 34.7 |
| 7 | 36.3 | 37.6 | 80.5 | 80.6 |
| 8 | 82.3 | 80.4 | 81.1 | 81.0 |
| 9 | 45.3 | 45.7 | 44.8 | 44.8 |
| 10 | 69.9 | 70.9 | 67.0 | 67.0 |
| 11 | 68.5 | 68.8 | 68.6 | 68.5 |
| 1′ | 98.1 | 97.3 | 97.0 | 97.0 |
| 2′ | 71.2 | 69.2 | 70.2 | 69.2 |
| 3′ | 72.4 | 68.6 | 71.4 | 68.5 |
| 4′ | 65.8 | 66.4 | 66.2 | 66.4 |
| 5′ | 75.3 | 70.3 | 74.1 | 70.2 |
| 6′ | 61.6 | 62.4 | 62.2 | 62.4 |

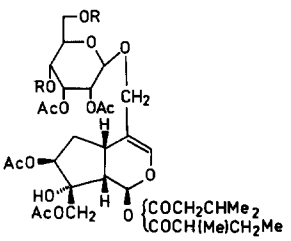
*Compound **1** showed signals from the isovaleroyl group at 173.2, 43.9, 26.3 and 22.4 ppm and from two acetyl groups at *ca* 175 and 21.0 ppm. Compound **1a** had corresponding signals.

†Data from ref. [4].

*Present address: Emulsion A/S, Juelsminde, Denmark.



1 R=H
1a R=Ac



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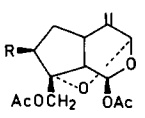
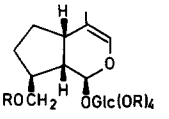
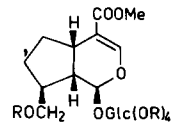
2a R Ac



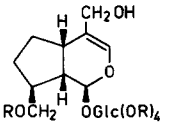
3 R=H
4 R=AcO



5 R=H
5a R=Ac



6 R=H
7 R=TMS



8 R=TMS
9 R=H

the structure given for decapetaloside [9, 10]*, yet with undetermined configuration at C-8. In the $^{13}C$ NMR spectra of **5** and **5a**, the shift values for C-10 (66.1 and 67.3 ppm) were closer to those of C-10 in adoxoside (**6**) and its penta-acetate (65.9 and 66.9 ppm) than to those of C-10 in the corresponding 8-epimers (63.4 and 65.0 ppm), cf. ref. [12], suggesting the 8β-configuration shown. However, in view of the small difference involved, a chemical correlation between **5** and **6** was undertaken. Trimethylsilylation of adoxoside (**6**), followed by reduction with lithium ethoxyaluminium hydride and desilylation, gave 11-hydroxydecapetaloside (**9**). Hydrogenolysis ($H_2$, Pd/C) of **9**, followed by acetylation, finally gave **5a**, indistinguishable from a specimen of natural derivation. This transformation proved the absolute structure of **5** to be as that depicted (cf. ref. [13]).

Iridoid glycosides with an allose moiety attached at C-11 have also been reported from *V. opulus* [4] and from two species of *Mentzelia* (Loasaceae) [11].

## EXPERIMENTAL

Microanalyses were performed at NOVO Microanalytical Laboratory, Bagsvaerd, Denmark. Material of *V. betulifolium* was collected in July 1977 in the Botanical Garden, The University of Copenhagen A voucher (IOK-62/77) has been deposited at the Botanical Museum, Copenhagen.

*Isolation of* **1** *from leaves.* Frozen (−23°) leaves (125 g) were extracted with EtOH essentially as described [4] to give fraction A (2.5 g) and fraction B (1.14 g). The latter was treated with activated C and fractionated on Sephadex G 15 with MeOH–$H_2O$ (4:1). The resulting fractions were monitored by TLC (silica gel, $CHCl_3$–MeOH, 4:1). The main iridoid fraction consisted of viburnalloside (**1**, 230 mg, 0.2%), isolated as a syrup after passage through activated C; $[\alpha]_D^{15}$ −86° (MeOH; *c* 1.4); $^1H$ NMR (90 MHz, $D_2O$, DSS): δ6.42 (*s (br)*, H-3), 6.16 (*d*, *J* = 3.5 Hz, H-1), 5.57 (*t (br)*, H-3'), 4.98 (*d*, *J* = 8.5 Hz, H-1'), 4.74 (*dd*, *J* = 3 and 8.5 Hz, H-2'), 4.25 (*s (br)*, 11-$CH_2$), 3.54 (*s (br)*, 10-$CH_2$), 2.76 (*m*, H-5), 2.20 and 2.04 (2 × OAc), 0.93 (*d*, *J* = 6 Hz, 2 × Me). (Found: C, 53.0; H, 6.8. $C_{25}H_{38}O_{13}\cdot H_2O$ requires: C, 53.2; H, 7.1%.)

*Acetylation of* **1** ($Ac_2O$–pyridine) gave a penta-acetate (**1a**) as a colourless syrup $[\alpha]_D^{25}$ −63° ($CHCl_3$; *c* 0.8); $^1H$ NMR (90 MHz, $CDCl_3$): δ6.39 (*s (br)*, H-3), 6.22 (*d*, *J* = 5 Hz, H-1), 5.66 (*t*, *J* = 2.4 Hz, H-3'), 4.75–5.05 (H-4', H-2' and H-1'), 3.94–4.33 (10-$CH_2$, 11-$CH_2$, H-5' and 6'-$CH_2$), 2.70 (*m*, H-5), 2.17, 2.13, 2.09 and 2.01 (1, 1, 1 and 2 × OAc), 0.98 (*d*, *J* = 7 Hz, 2 × Me). (Found: C, 55.0; H, 6.6. $C_{31}H_{44}O_{16}$ requires: C, 55.4; H, 6.6%.)

*Cleavage of* **1a**. The procedure used earlier [4] proved unsatisfactory, as supposedly dimeric aglucone derivatives were formed. Instead, the following procedure was adopted. To **1a** (430 mg) in $Et_2O$ (10 ml) at −20° was added $BF_3\cdot Et_2O$ (1 ml) with stirring. After 7 min, $Ac_2O$ (3 ml) was added and then after 5 min pyridine (2 ml) and ice (20 g) to quench the reaction. The mixture was worked up after 2 hr, i.e. the organic phase was washed with dilute $H_2SO_4$, then saturated $NaHCO_3$, dried and concd to give crude product (385 mg). Prep. TLC (silica gel, pentane–$Me_2CO$, 2:1) provided as the faster moving band **3**, (28 mg), a syrup, $[\alpha]_D^{14}$ +41° ($CHCl_3$; *c* 0.2); $^1H$ NMR (90 MHz, $CDCl_3$): δ6.35 (*d*, *J* = 3 Hz, H-1), 5.12 (*s*, H-3), 4.92 (*m*, 11-$CH_2$), 4.35 and 4.10 (AB, *J* = 12 Hz, 10-$CH_2$), 2.11 and 2.04 (2 × OAc). (Found: C, 59.3; H, 6.5. $C_{14}H_{18}O_6$ requires: 59.6; H, 6.4%.) The slower moving fraction (187 mg) consisted of a mixture and was rechromatographed ($Et_2O$–pentane, 2:1). The faster moving fraction (39 mg) gave penta-*O*-acetyl-β-D-allopyranose, identical to an authentic sample (mp and $[\alpha]_D$), while the slower fraction (107 mg) appeared ($^1H$ NMR) to be a dimeric aglucone derivative.

*Isolation of decapetaloside* (**5**) *from bark.* Frozen bark and twigs (250 g) were homogenized with EtOH and worked up as described earlier [14] to give crude glycosides (4.7 g). Chromatography on silica gel (300 g) with $CHCl_3$–MeOH (8:1 to 4:1) gave a main fraction (1.8 g, 0.7%) of almost pure decapetaloside (**5**). Rechromatography afforded an analytical sample as a syrup, $[\alpha]_D^{15}$ −71° (MeOH; *c* 5.0) $^1H$ NMR (90 MHz, $D_2O$): δ6.09 (*s (br)*, H-3), 5.14 (*d*, *J* = 4 Hz, H-1), 3.58 (*d (br)*, *J* = 6 Hz, 10-$CH_2$), 2.51 (*m*, H-5), 1.56 (*s (br)*, 11-Me). (Found: C, 52.4; H, 8.0. $C_{16}H_{26}O_8\cdot H_2O$ requires: C, 52.7; H, 7.8%.) The $^{13}C$ NMR spectrum has been published [12].

*Acetylation of* **5** produced the crystalline penta-acetate (**5a**) (EtOH), mp 113–114°; $[\alpha]_D^{24}$ −92° ($CHCl_3$; *c* 0.15) (lit. [9] mp 114–115°; $[\alpha]_D^{22}$ −90° ($CHCl_3$; *c* 3.7)); $^1H$ NMR (90 MHz, $CDCl_3$): 5.95 (*s (br)*, H-3), 5.19 (*s (br)*, partly obscured, H-1), 4.01 (*d*, *J* = 6 Hz, 10-$CH_2$), 2.5 (*m*, H-5), 2.10–1.98 (5 × OAc), 1.49 (*s (br)*, 11-Me). (Found: C, 56.3; H, 6.6. $C_{26}H_{36}O_{13}$ requires: C, 56.1; H, 6.5%.) The $^{13}C$ NMR spectrum has been published [12].

*Trimethylsilylation of adoxoside.* Adoxoside (**6**) (0.35 g), isolated from *V. carlesii* [7], was dissolved in pyridine (10 ml), and hexamethyldisilazane (4 ml) and trimethylsilyl chloride (2 ml) were added. After 30 min, work-up provided the silylated derivative **7** as an oil (0.82 g). $^1H$ NMR (90 MHz, $CDCl_3$). δ7.50 (*s*, H-3), 4.96 (*d*, *J* = 8 Hz, H-1), 4.65 (*d*, *J* = 7 Hz, H-1'), 3.75 (*s*, OMe), 3.00 (*q (br)*, *J* = 7 Hz, H-5)

*Reduction of* **7** (0.82 g) was performed in $Et_2O$ (25 ml) with

*Data for **5** were published by one of us in 1978 [7], and the name mongolioside was later introduced for the compound isolated from another source [11]. However, in order to avoid further confusion in the literature, we suggest that the name decapetaloside acquires priority. Consequently, the name of the compound '10-*O*-acetyl-6β-hydroxy-mongolioside' [12] should be changed to 10-*O*-acetyl-6β-hydroxydecapetaloside.

$LiAlH_3(OEt)$ (prepared from 130 mg $LiAlH_4$ in 6 ml $Et_2O$ to which 157 mg EtOH was added) during 4 hr. The reaction was terminated by adding $H_2O$ (10 ml), and the resulting mixture was extracted with $CH_2Cl_2$. Evapn gave an oil (0.54 g) of apparently pure **8**, as seen by the $^1H$ NMR spectrum (90 MHz, $CDCl_3$): $\delta$6.27 (*s* (*br*), H-3), 5.17 (*s* (*br*), OH), 4.85 (*d*, $J$ = 8 Hz, H-1), 4.62 (*d*, $J$ = 6.5 Hz, H-1'), 4.06 (*m*, 11-$CH_2$).

11-*Hydroxydecapetaloside* (**9**). Hydrolysis of **8** (0.38 g) was achieved by stirring in MeOH at room temp. for 96 hr, while $H_2O$ was added successively. Evapn followed by prep. TLC gave **9** (130 mg) as a syrup, $[\alpha]_D^{23}$ −99° (MeOH; *c* 0.2); $^1H$ NMR (90 MHz, $D_2O$): $\delta$6.33 (*s* (*br*), H-3), 5.22 (*d*, $J$ = 3.5 Hz, H-1), 4.08 and 3.89 (AB, $J$ = 12 Hz, 11-$CH_2$), 2.72 (*m*, H-5). (Found: C, 48.7; H, 7.6. $C_{16}H_{26}O_9 \cdot H_2O$ requires: C, 48.3; H, 7.6%.) The $^{13}C$ NMR spectrum has been published [12].

*Reduction of* **9**. The alcohol (**9**) (11 mg) in MeOH (2 ml) with 5% Pd/C (5 mg) was stirred under $H_2$ for 6 min. Acetylation of the product afforded crude **5a** (20 mg). Prep. TLC and crystallization (EtOH) gave pure **5a** (5 mg), mp 111.5–112°, mmp 111–112.5° with the product obtained from *V. betulifolium*.

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