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TWO IRIDOIDS FROM *VIBURNUM LANTANA*

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Key Word Index—*Viburnum lantana*; Caprifoliaceae; iridoids; 2′-*O*-acetyldihydropenstemide; 2′-*O*-acetylpatrinoside.

Abstract—Two new iridoids with an isovaleroyl group at C-1 and a sugar moiety at C-11 have been isolated from the bark of *Viburnum lantana*. Their structures were characterized as 2′-*O*-acetyldihydropenstemide and 2′-*O*-acetylpatrinoside by spectroscopic and chemical means.

INTRODUCTION

Viburnum species are used in folk and official medicine as uterotonic, chemostatic, sedative and diuretic drugs [1]. They are a source of iridoid compounds [2–10], two new ones of which we have isolated from the previously unstudied species *V. lantana*.

RESULTS AND DISCUSSION

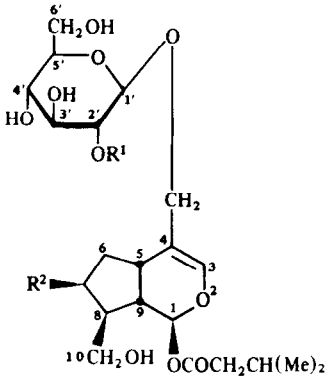
Compounds **1** and **2** were isolated from the dried bark of *V. lantana*. Both compounds after heating with dilute hydrochloric acid produced a dark resinous product, typical for iridoids, and afforded glucose [TLC and GC (silylated derivative)].

Compound **1** exhibited IR absorption bands at 3450 (hydroxyl groups), 1730–1750 (ester group), 1670 (double bond) and 1250 cm^{-1} (acetoxy group). Its ^1H and ^{13}C NMR spectra were similar to those of dihydropenstemide (**3**) [4,11] with the exception of the signals for one acetoxy group, indicating that **1** was a monoacetate of **3** (Table 1).

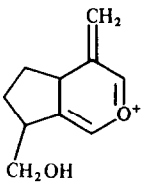
Acetylation of **1** provided a penta-acetate (**1a**), the M_r mass (656) of which as determined by CIMS (Et_2NH) [12, 13] showed **1** to have a M_r of 488. The presence of two intense peaks at *m/z* 422 (60%) $[gluAc_4 + 74]^+$ and at 298 (50%) $[M + Et_2NH_2 - 102 - 330]^+$ characterized the sugar and the aglycone parts (Scheme 1).

Furthermore, comparison of the ^{13}C NMR spectra of **1a** and dihydropenstemide penta-acetate **3a** showed their common identity (Table 2). The site of esterification was established by comparison of the ^1H and ^{13}C NMR spectra of **1** with those of **3**. The ^1H NMR spectrum of **1** indicated that the acetoxy residue was linked to the glucose moiety. No shift of the methylene protons at C-10 (δ3.53) was observed while the H-2′ signal showed a considerable paramagnetic shift (δ4.70 cf δ3.18 for **3**) (Table 1). The C-2′ position of the acetoxy group was supported also by the low field shifts of the C-1′ and C-3′ signals in the ^{13}C NMR spectrum of **1** compared to those of dihydropenstemide (**3**).

The EIMS (12 eV) of **1** was in agreement with the proposed structure of the aglycone. Signals with *m/z* 165 and 164 being due to the aglycone of **1** after elimination of isovaleric acid and either water or a hydroxyl group. The



	R^1	R^2
1	Ac	H
2	Ac	OH
3	H	H
4	H	OH



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m/z 165(85)

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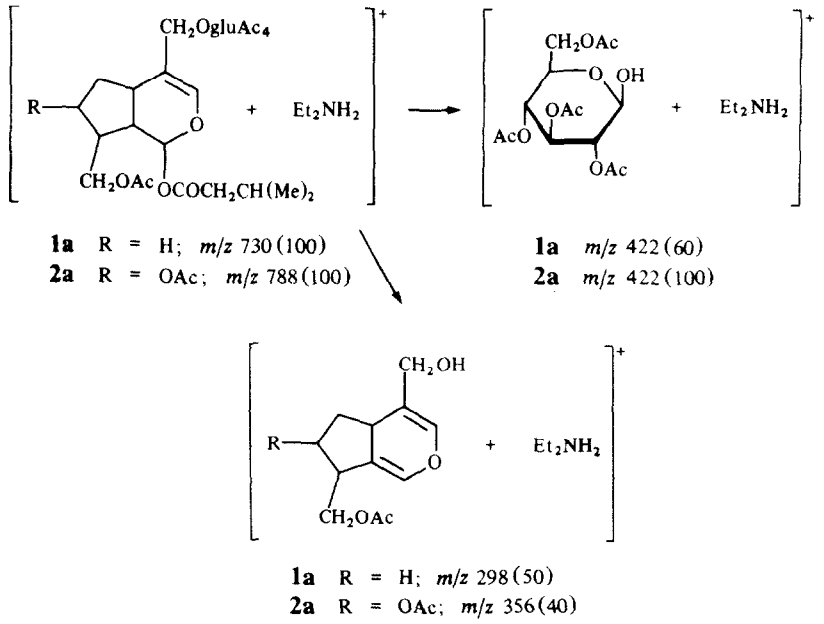

Scheme 1. CIMS (Et_2NH) fragmentation of compounds **1a** and **2a**.

Table 1. ^1H NMR data of

H	1*	3†	1a‡
1	5.99 *d* (4.5)	5.96 *d* (4.6)	5.94 *d* (5.5)
3	6.32 *br s*	6.37 *br s*	6.32 *d* (1.5)
5	2.70 *m q-habitus*	2.82 *m q-habitus*	2.67 *m q-habitus*
6	1.82 *m*	1.39 *m*	1.6 *m*
	1.69 *m*	1.70 *m*	1.7–2.1 *m*
7	1.9–2.2 *m*	1.90–2.02 *m*	1.7–2.1 *m*
	1.40 *m*	1.82 *m*	1.34 *m*
8	1.9–2.2 *m*	1.90–2.02 *m*	2.17 *m*
9	1.9–2.2 *m*	1.90–2.02 *m*	2.10 *m*
10	3.53 *d* (6.0)	3.52 *d* (6.0)	4.04 *d* (7.0)
11	4.21 *d* AB (12.0)	4.16 *d* AB centre	4.04 *d* AB (12.0)
	4.04 *d* AB (12.0)	(11.5)	4.20 *d* AB (12.0)
1′	4.46 *d* (8.0)	4.28 *d* (7.7)	4.54 *d* (8.0)
2′	4.70 *dd* (8.0; 9.0)	3.18 *dd* (7.8; 9.1)	5.02 *dd* (8.0; 9.5)
3′	3.53 *t* (9.0)		5.22 *t* (9.5)
4′	3.35‖		5.08 *t* (9.5)
5′	3.28‖		3.69 *m*
6′	3.88 *dd* AB from ABX (12.0; 2.2)	3.86 AB from ABX (11.7; 1.8)	4.26 *dd* AB from ABX (11.5; 5.0)
	3.68 *dd* AB from ABX (12.0; 5.5)	3.65 AB from ABX (11.7; 5.4)	4.14 *dd* AB from ABX (11.5; 2.5)
MeCO-isovaleroyl	2.1 *s*		
–CH<	1.9–2.2 *m*	2.07	1.7–2.1 *m*
$-CH_2-$	2.23 *d*	2.22	2.25 *d*
$(CH_3)_2$	0.96 *d*	0.96 *d*	0.98 *d*

*1 and 2 in CD_3OD, 250 MHz.
†3 in CD_3OD, 400 MHz, ref. [11].
‡1a and 2a in $CDCl_3$, 250 MHz.
§4a in $CDCl_3$, 100 Hz, ref. [15].
‖Partially covered by the solvent signal.

presence of the isovaleroyl and acetyl moieties in the molecule was shown by the intense peaks at *m/z* 85, 57, 60 and 43 in the EIMS (70 eV) of **1**.

The stereochemistry at C-8 of compound **1** (C-9, δ45.0; C-10, 66.6; H-1, 5,96) was studied by ^{13}C NMR [14] and by comparison of the ^{13}C and ^{1}H NMR data with those of dihydropenstemide **3** (C-9, δ44.95; C-10, 66.48; H-1, 5.96) [11] and 8-epidihydropenstemide (C-9, δ42.71; C-10, 64.29; H-1, 6.26) [11]. All the data were consistent with an 8-β-CH_2OH substituent. Thus compound **1** was identified as 2′-*O*-acetyldihydropenstemide.

On the basis of decoupling experiments on the ^{1}H NMR spectrum of compound **1**, we found that the published shifts for H-6 and H-7 in the ^{1}H NMR spectrum of dihydropenstemide [11] should be changed as follows: H-6, δ1.69 and 1.82; H-7, δ1.4 and 1.9–2.2.

Compound **2** had a similar IR spectrum to that of compound **1** (3450, 1730–1750, 1670, 1260 cm^{-1}). Acetylation afforded a hexa-acetate (**2a**) with a M_r of 714 (CIMS with Et_2NH). The ^{1}H NMR spectrum of **2** showed the presence of one acetoxy group and hence a M_r of 504 for **2**. The MS fragmentation of compound **2** resembled that of the penta-acetate of 2′-*O*-acetyldihydropenstemide (**1a**) (Scheme 1 and Experimental).

Comparison of the ^{13}C NMR data of the hexa-acetate of compound **2** and an authentic sample of patrinoside hexa-acetate (**4a**) [4, 14, 15] confirmed the identity of both compounds (Table 2). As with 2′-*O*-acetyldihydropenstemide (**1**), the ^{1}H NMR data showed that the acetoxy group in compound **2** was not attached at the aglycone, i.e. H-10 and H-7 signals unchanged (Table 1). A 2′-location of the acetoxy group in the glucosidic moiety was determined on the basis of the same considerations as in the case of compound **1** (Tables 1 and 2).

The similar ^{1}H and ^{13}C NMR spectra of compound **2** and patrinoside (**4**) proved that the former contained 7-β-OH and 8-β-CH_2OH groups. Compound **2** was thus identified as 2′-*O*-acetylpatrinoside.

EXPERIMENTAL

^{1}H NMR (250 MHz) and ^{13}C NMR (62.9 MHz): solvents as indicated with TMS as int. standard (accuracy $\pm$0.25 Hz).

Extraction and isolation. Dried powdered bark of *Viburnum lantana* (750 g) from Mount Vitosha was extracted with 5 l $CHCl_3$ and 3 × 5 l MeOH. The MeOH extracts were bulked and the solvent removed to give a residue (42 g) which was dissolved in H_2O and successively extracted with Et_2O, EtOAc and BuOH. The EtOAc extract was concd to dryness to give a residue (7 g) which was applied to a silica gel column. Elution with $CHCl_3$–MeOH (8:1) with increasing MeOH content gave impure compounds **1** and **2**, which were repeatedly chromatographed until pure.

compounds **1–3**, **1a**, **2a** and **4a**

2*	2a‡	4a§
5.93 *d* (5.0)	5.92 *d* (5.3)	5.86 *d* (6)
6.31 *br s*	6.33 *d* (1.5)	6.25 *d* (1.5)
2.89 *m q-habitus*	2.88 *m q-habitus*	2.7–3.2 *m*
1.80 *m*	1.9 *m*	2.2
1.97 *m*	1.9–2.3 *m*	
4.31 *m*	5.27 *m*	
1.90–2.10 *m*	1.9–2.3 *m*	
2.18 *m*	1.9–2.3 *m*	
3.83 *dd* AB from ABX (10.0; 6.0)	4.18 *m*	4.05–4.20
3.71 *dd* AB from ABX (10.0;7.5)		
4.22 *d* (11.0)	4.20 *d* AB (11.5)	
4.05 *d* (11.0)	4.06 *d* AB (11.5)	
4.46 *d*	4.52 *d* (8.0)	
4.71 *dd* (11.0)	5.02 *dd* (8.0; 9.5)	
3.52 *t* (9.0)	5.21 *t* (9.5)	
3.35‖	5.05 *t* (9.5)	
3.27‖	3.70 *m*	
3.88 *dd* AB from ABX (12.0; 2.0)	4.26 *dd* ABX (11.0; 5.0)	
3.67 *dd* AB from ABX (12.0; 4.5)	4.15 *dd* AB (11.0; 2.5) from ABX	
2.10 *s*		
1.9–2.1 *m*	1.9–2.3	1.95–2.10
2.24 *d*	2.27	
0.96 *d*	0.98 *d*	0.96 *d* (6)

Table 2. ^{13}C NMR data of compounds **1**–**4** and **1a**–**4a**

C	1*	3†	1a‡	3a§	2*	4¶	2a‡	4a‖
1	92.9	93.2	91.4	91.0	93.5	93.5	91.3	90.8
3	140.7	140.6	140.4	140.0	140.1	139.9	140.1	139.7
4	114.5	115.2	112.2	111.7	116.2	115.7	112.7	112.2
5	36.8	36.9	36.1	35.6	34.0	33.4	33.1	32.7
6	30.6	30.9	30.1	29.5	41.0	39.9	37.5	37.0
7	28.0	28.1	27.4	26.9	73.5	72.3	74.1	73.5
8	44.2	43.9	39.1	38.6	49.0	48.1	43.2	42.7
9	45.0	45.0	43.8	43.3	41.0	41.5	42.2	41.7
10	66.6	66.5	67.3	66.8	62.3	61.5	62.5	62.0
11	69.6	69.6	69.0	68.5	69.8	69.6	68.8	68.8
1′	102.2	103.5	99.3	98.8	101.3	102.0	99.2	98.6
2′	75.4	75.2	71.4	70.9	75.5	73.9	71.4	70.8
3′	76.3	77.9	72.0	71.4	76.3	76.6	72.0	71.5
4′	71.9	71.8	68.0	68.0	71.9	70.4	68.5	68.0
5′	78.1	78.2	73.0	72.5	78.2	76.6	73.0	72.5
6′	62.8	62.9	62.0	61.5	62.8	61.5	62.0	61.5
isovaleroyl								
>C=O	173.4	173.5	171.9		173.5		171.8	
$-CH_2-$	44.2	44.2	43.3		44.3		43.2	
-CH<	26.8	26.8	25.6		26.9		25.6	
-Me × 2	22.6	22.6	22.3		22.7		22.3	
acetyl								
>C=O	171.7				172.0			
Me	21.7				21.2			

1 and **2** in CD_3OD, 62.9 MHz
†**3** in CD_3OD, 100 MHz, ref. 11
‡**1a** and **2a** in $CDCl_3$, 62.9 MHz
§**3a** in $CDCl_3$, 22.6 MHz, ref. 4.
¶**4** in D_2O, 22.6 MHz, ref. 14.
‖**4a** in $CDCl_3$, 22.6 MHz, ref. 14.

2′-O-Acetyldihydropenstemide (**1**). Amorphous powder (94 mg). UV λ_{max}^{MeOH} nm: 212; IR ν_{max}^{film} cm^{-1}: 3450, 1730–1750, 1670, 1375, 1250, 1090, 765; ^1H NMR (250 MHz, CD_3OD, decoupling experiments), see Table 1; ^{13}C NMR (62.9 MHz, CD_3OD, DEPT technique), see Table 2; EIMS (70 eV), *m/z* (rel. int.): 207 (10), 206 (12), 165 (40) $[M-102-221]^+$, 164 (50) $[M-102-222]^+$, 85 (80), 60 (45), 57 (65), 43 (100); EIMS (12 eV): 249 (11) $[M-222-17]^+$, 207 (20), 205 (22) $[221-17]^+$, 165 (85) $[M-102-221]^+$, 164 (55), 85 (70), 60 (30), 57 (60), 43 (20).

Acetylation of **1**. Compound **1** (52 mg) was treated with pyridine–Ac_2O in the usual manner. The resultant acetate was purified by silica gel CC to give 45 mg of the pentaacetate **1a**, $C_{31}H_{44}O_{15}$, mp 97–99°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1670, 1375, 1250, 1050, 765; ^1H NMR (250 MHz, $CDCl_3$), see Table 1. ^{13}C NMR (62.9 MHz, $CDCl_3$), see Table 2. CIMS (Et_2NH), *m/z* (rel. int.): 730 (100) $[M+74]^+$, 422 (60) $[348+74]^+$, 298 (50) $[730-102-330]^+$; EIMS (70 eV): 331 (40), 207 (70) $[M-102-347]^+$, 206 (72), 169 (50), 109 (20), 85 (60), 57 (60), 43 (100); EIMS (12 eV): 207 (100), 206 (100), 169 (100), 147 (25), 109 (20), 85 (35), 57 (10), 43 (12).

Acid hydrolysis of **1**. Compound **1** (5 mg) was dissolved in 1 ml 0.5 M H_2SO_4, and the mixture refluxed for 1 hr. After neutralization and removal by filtration of the resinous products, the H_2O soln was concd. D-Glucose was identified by TLC (EtOAc–pyridine–H_2O 2:1:2) and GC of the silylated derivative.

2′O-Acetylpatrinoside (**2**). Hydroscopic amorphous powder (97 mg). UV λ_{max}^{MeOH} nm: 212; IR ν_{max}^{film} cm^{-1}: 3450, 1750, 1670, 1375, 1260, 1080, 765; ^1H NMR (250 MHz, CD_3OD, decoupling experiments), see Table 1; ^{13}C NMR (62.9 MHz, CD_3OD, DEPT technique for multiplicity), see Table 2. EIMS (70 eV), *m/z* (rel. int.) 402 (1) $[M-102]^+$, 384 $[M-102-18]^+$, 342 (18) $[M-102-60]^+$, 181 (20) $[M-102-221]^+$ 180 (20), 85 (80), 60 (48), 57 (54), 43 (100).

Acetylation of **2**. Compound **2** was acetylated with pyridine–Ac_2O and the acetylated product purified by silica gel chromatography to give the hexa-acetate **2a** (67 mg), $C_{33}H_{46}O_{17}$, mp 129–131°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1665, 1435, 1375, 1250, 1050, 770; ^1H NMR (250 MHz, $CDCl_3$), see Table 1. ^{13}C NMR (62.9 MHz, $CDCl_3$), see Table 2. CIMS (Et_2NH), *m/z* (rel. int.): 788 (82) $[M+74]^+$, 422 (100) $[348+74]^+$, 356 (40) $[788-102-330]^+$; EIMS (70 eV): 383 (4) $[M-331]^+$, 331 (20), 273 (10), 265 (1), 264 (10), 169 (70), 153 (20), 144 (20), 109 (25), 85 (70), 57 (50), 43 (100).

Acid hydrolysis of **2**. 6 mg of compound **2** was refluxed with 1 ml 0.5 M H_2SO_4 for 1 hr. After neutralization and removal of the resinous products by filtration, the water phase was concentrated and D-glucose was identified by TLC and GC of the silylated derivative.

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