Pergamon

S0031-9422(96)00143-4

Phytochemistry, Vol. 42, No. 5, pp. 1435–1438, 1996

0031-9422/96 $15.00 + 0.00

A NEOLIGNAN GLYCOSIDE AND ACYLATED IRIDOID GLUCOSIDES FROM STEM BARK OF *ALANGIUM PLATANIFOLIUM*

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(*Received in revised form* 23 *January* 1996)

Key Word Index—*Alangium platanifolium* var. *trilobum*; Alangiaceae; neolignan glycoside; alangiplatanoside; iridoid glucoside acyl ester; loganic acid.

Abstract—From the stem bark of *Alangium platanifolium* var. *trilobum*, alangiplatanoside, a neolignan 2-*O*-(β-apiofuranosyl)-β-glucopyranoside, and the *E*- and *Z*-ferulic esters of loganic acid were isolated. Their structures were determined by spectroscopic methods.

INTRODUCTION

In our continuing studies of Alangiaceae [1, 2], stem bark of *Alangium platanifolium* Harms var. *trilobum* Ohwi was investigated. Alangiplatanoside, a neolignan β-apiofuranosyl (1‴→2″)-β-glucopyranoside (**1**), and 7-*O*-*E*- and 7-*O*-*Z*-feruloylloganic acids (**2** and **3**) along with a known compound, henryoside, were isolated [3]. This paper deals with the structural elucidation of these new compounds.

RESULTS AND DISCUSSION

Compound **1**, $[\alpha]_D$ −77.1°, was obtained as an amorphous powder whose elemental composition was analysed for $C_{31}H_{42}O_{15}$ on the basis of the observation of the observation of a quasimolecular ion peak in its negative ion high-resolution FAB mass spectrum. The ^{13}C NMR signals included five aromatic signals with protons (two singlets and three protons in an ABX coupling system in the ^1H NMR spectrum) and seven aromatic signals with substituents, four of which must carry electronegative substituents judging from their chemical shifts. Two methylene, two methine, [δ_C 55.5 and 88.4 with δ_H 5.53 (*d*, $J = 5$ Hz)], two primary carbinol and two methoxyl carbon signals were also observed. Of the remaining 11 signals, five could be assigned to a terminal β-apiofuranosyl unit (Table 1) and six to a β-glucopyranosyl moiety. The presence of these sugars was confirmed by GC analysis. The former was attached to C-2 in the latter as seen by the lowfield shift (*ca* 4 ppm) of this carbon when compared to the data reported for dihydrodehydrodiconiferyl alcohol 4′-*O*-β-D-glucoside [4] and also confirmed in a NOESY experiment by a cross peak between H-1‴ and H-2″. The phenolic alcohol at C-4′ must participate in the glycosidic linkage, since on irradiation of the anomeric proton (δ_H 4.98), a significant NOE enhancement was observed in the aromatic proton at H-5′ in the difference NOE experiment. The relative orientation of the substituents at the 7′- and 8′-positions were determined to be *trans* from the observation of cross peaks between H-7′ and H-9′a, and H-8′ and H-2′ in the NOESY spectrum. The absolute stereochemistry at the 7′- and 8′-positions were shown to be *R* and *S*, respectively, from the circular dichroic spectrum showing a negative Cotton effect at 278 nm ($\Delta\varepsilon$ −1.3) [5]. Therefore, the structure of **1** is taken to be as shown in the formula.

Compound **2**, $[\alpha]_D$ −30.5°, was obtained as an off-white amorphous powder. Negative ion HR-FAB mass spectral analysis revealed its elemental composition to be $C_{26}H_{32}O_{13}$. The IR and UV spectra indicated the presence of benzene rings (1590 and 1510 cm^{-1}), and conjugated double bonds (1670 and 1625 cm^{-1} and 235 nm). The ^1H spectrum showed the presence of three olefinic protons attributable to a *trans* double bond and an enol ether, three aromatic protons coupled in an ABX system and two hemiacetalic protons. The ^{13}C NMR spectrum with 26 peaks showed the presence of a feruloyl moiety and a loganic acid moiety. When compared with data published [6] for loganic acid (**4**) and periclymenoside as well as for periclymenosidic acid [7], the feruloyl group had to be attached to the 7-oxygen of the loganic acid moiety due to the downfield shifts of H-7 and C-7 in **2**. The compound is therefore 7-*O*-*E*-feruloylloganic acid. Although 7-*O*-(4″-*O*-β-D-glucopyranosyl-*E*-feruloyl)loganic acid (periclymenosidic acid) is a known compound obtained from *Lonicera coerulea* [7], 7-*O*-*E*-feruloylloganic acid seems to have been isolated from a natural source for the first time.

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Table 1. ^{13}C NMR data for alangiplatanoside (**1**), compounds **2**, **3** and loganic acid (**4**) (100 MHz, CD_3OD)

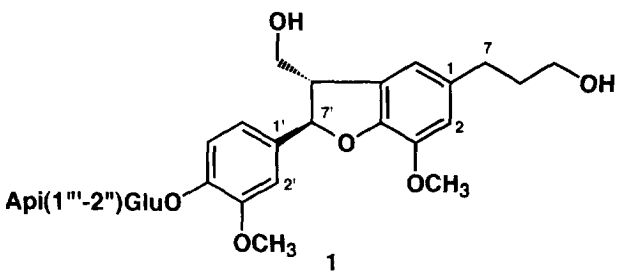
C	1	2	3	4*
1	129.5 (130.0)‡	97.7	97.6	97.6
2	114.1 (113.6)	—	—	—
3	145.1 (144.7)	152.7	152.7	152.0
4	147.4 (147.3)	113.3	113.4	114.2
5	138.2 (136.3)	32.9	32.7	32.7
6	117.9 (117.5)	40.5	40.5	42.6
7	32.8 (32.7)	78.5	78.4	75.0
8	35.7 (36.0)	41.2	41.0	42.0
9	62.2 (61.5)	47.2	47.1	46.4
10		13.9	13.8	13.5
11		170.8	170.7	171.4
1′	136.9 (136.9)	100.3	100.2	99.9
2′	111.2 (110.9)	74.8	74.8	74.6
3′	147.4 (147.2)	78.5	78.4	77.9
4′	150.7 ( )§	71.7	71.7	71.4
5′	117.9 (116.3)	78.1	78.1	78.1
6′	119.3 (118.8)	62.8	62.8	62.7
7′	88.4 (87.8)			
8′	55.5 (55.1)			
9′	65.7 (64.4)			
1″	100.9 (100.4)	127.4	128.4	
2″	78.8 (79.1)	111.8	114.9	
3″	77.5 (76.6)	150.7	149.4	
4″	71.5 (71.4)	149.4	148.4	
5″	77.9† (78.0)	114.9	115.8	
6″	62.5 (62.2)	124.2	126.3	
7″		146.8	145.4	
8″		116.5	117.2	
9″		168.9	168.1	
1‴	111.1 (110.3)			
2‴	78.0† (78.7)			
3‴	80.5 (81.0)			
4‴	75.0 (75.8)			
5‴	65.0 (66.4)			
-OMe	56.4 (55.9)	56.5	56.5	
	56.8 (56.3)			

*Data taken from ref. [6].

†Assignments may be interchanged.

‡Chemical shifts in parentheses are for pyridine-d_5.

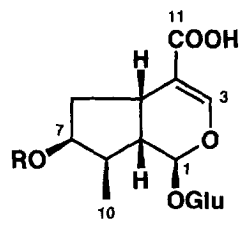
§Overlapped by the solvent signal.



1

Glu : β-glucopyranosyl (1″-6″)

Api : β-apiofuranosyl (1‴-5‴)



R

2 *E*-ferulic acid (1″-9″)

3 *Z*-ferulic acid (1″-9″)

4 H

Glu : β-D-glucopyranosyl (1′-6′)

The spectroscopic data showed compound **3** to be an isomer of 2. However, the coupling constants of two olefinic protons [δ_H 5.80 (*d*, $J = 13$ Hz) and 6.88 (*d*, $J = 13$ Hz)] in the ^{1}H spectrum led to the conclusion that **3** is 7-*O*-*Z*-feruloylloganic acid.

EXPERIMENTAL

General. ^{1}H and ^{13}C NMR (TMS as int. standard): 400 and 100 MHz, respectively; EIMS: 70 eV.

Plant material. Stems of *A. platanifolium* var. *trilobum* were collected in Shimane Prefecture in 1988. A voucher specimen was deposited in the Herbarium of the Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine (APT-88-Shimane).

Extraction and isolation. Air-dried stem bark (1.27 kg) was thoroughly extracted with MeOH. The MeOH extract was concd to 1.5 l, and 75 ml H_2O was added to make a 95% aq. MeOH soln. This soln was extracted with *n*-hexane (1.5 l, 11.0 g of extract) and then the MeOH layer was evapd to leave a residue. The residue was suspended in H_2O (1 l) and then extracted with EtOAc (1 l, 12.7 g of extract) and *n*-BuOH (1.5 l, 20.6 g of extract) successively (residue 51.3 g). The *n*-BuOH extract was dissolved in 1 l of 20% MeOH in H_2O, and then subjected to CC on a highly porous synthetic resin (Diaion HP-20, 5.5 cm × 40 cm) with the solvent systems MeOH–H_2O [(1:4, 2 l), (2:3, 3 l), (3:2, 3 l), (4:1, 3 l) and MeOH (3 l)], 500-ml frs being collected. The residue (2.40 g) of frs 13–15 was subjected to silica gel (180 g) CC with the solvent system $CHCl_3$–MeOH–H_2O [150:15:0.1 (3.3 l), 150:30:0.1 (3.6 l), 150:60:0.1 (3.2 l), 75:30:0.1 (2.1 l), and 30:12:0.1 (2.1 l), 500 ml frs being collected]. The residue (190 mg) of frs 51–62 was subjected to DCCC [500 glass columns (2 mm × 40 cm); $CHCl_3$–MeOH–H_2O–*n*-PrOH (9:12:10:2, 4-g frs being collected), fractions were numbered according to the elution of the mobile phase]. Henryoside (15 mg) was recovered in frs 37–47, and the residue (82 mg) of frs 51–69 was finally purified by prep. HPLC [ODS (Inertsil), 20 × 250 mm, H_2O–MeOH (3:1), 6 ml min^{-1}, R_t 39 min] to give 34 mg **1**.

The residue (1.30 g) of frs 16–19 obtained on Diaion HP-20 CC was subjected to silica gel (150 g) CC with the solvent system $CHCl_3$–MeOH–H_2O [150:15:0.1 (3.3 l), 150:30:0.1 (3.6 l), 150:60:0.1 (4.2 l), 75:30:0.1 (2.1 l), 30:12:0.1 (2.1 l) and 150:60:1 (2.1 l), 500-ml frs being collected]. The residue (420 mg) of frs 22–32 was further sepd by DCCC to give 96 mg of a mixt. of **2** and **3**. A portion of the fr. (55 mg) was purified by prep. HPLC with MeOH–H_2O (9:11) containing 0.1% TFA to afford 43 mg **2** (R_t 52.5 min) and 8.5 mg **3** (R_t 48.5 min).

From the residue (1.84 g) obtained from frs 9–12 from Diaion HP-20 CC, a further 50 mg henryoside was obtained in a similar manner.

Known compounds isolated. Henryoside, $[\alpha]_D^{25}$ −21.5° (pyridine, *c* 0.54), other spectroscopic data were essentially the same as the reported values [3].

Alangiplatanoside (**1**). Amorphous powder, $[\alpha]_D^{25}$ −77.1° (MeOH, *c* 1.66). UV λ_{max}^{MeOH} nm (log ε): 213 (4.35), 226 (4.43)sh, 281 (3.73); ^{1}H NMR (CD_3OD): δ 1.80 (2H, *qui*, $J = 7$ Hz, H_2-8), 2.62 (2H, *br t*, $J = 7$ Hz, H_2-7), 3.45 (H, *br q*, $J = 6$, H-8′), 3.54 (H, *d*, $J = 11$ Hz, H-5‴a), 3.58 (H, *d*, $J = 11$ Hz, H-5‴b), 3.70 (H, *dd*, $J = 8$, 9 Hz, H-2″), 3.74 (H, *dd*, $J = 7$, 11 Hz, H-9′a), 3.79 (3H, *s*, -OMe on C-3), 3.84 (H, *dd*, $J = 5$, 11 Hz, H-9′b), 3.85 (3H, *s*, -OMe on C-3′), 3.97 (H, *d*, $J = 1$ Hz, H-2‴), 4.16 (H, *d*, $J = 10$ Hz, H-4‴b), 4.98 (H, *d*, $J = 8$ Hz, H-1″), 5.53 (H, *d*, $J = 5$ Hz, H-7′), 5.54 (H, *d*, $J = 1$ Hz, H-1‴), 6.71 (H, *br s*, H-2), 6.72 (H, *br s*, H-6), 6.99 (H, *dd*, $J = 2$, 8 Hz, H-6′), 7.00 (H, *d*, $J = 2$ Hz, H-2′), 7.07 (H, *d*, $J = 8$ Hz, H-5′); ^{13}C NMR (CD_3OD): Table 1; CD (MeOH, *c* 0.00498): $\Delta\varepsilon$ (nm): −2.6 (214), −2.0 (237), −1.3 (278); HR-FAB-MS (negative centroid) *m/z*: 653.2473 $[M-H]^-$ ($C_{31}H_{41}O_{15}$ requires 653.2445).

7-O-E-*Feruloylloganic acid* (**2**). Amorphous powder, $[\alpha]_D^{25}$ −30.5° (MeOH, *c* 0.85). IR ν_{max}^{KBr} cm^{-1}: 3300, 1670, 1625, 1590, 1510, 1425, 1270, 1150, 1075; UV λ_{max}^{MeOH} nm (log ε): 222 (4.14)sh, 235 (4.17), 305 (4.07)sh, 325 (4.13); ^{1}H NMR (CD_3OD): δ 1.10 (3H, *d*, $J = 7$ Hz, H_3-10), 1.81 (H, *ddd*, $J = 5$, 8, 14 Hz, H-6β), 2.10 (H, *dt*, $J = 5$, 8 Hz, H-9), 2.21 (H, *m*, H-8), 2.36 (H, *ddd*, $J = 1$, 8, 14 Hz, H-6α), 3.15 (H, *br q*, $J = 8$ Hz, H-5), 3.22 (H, *dd*, $J = 8$, 9 Hz, H-2′), 3.39 (H, *t*, $J = 9$ Hz, H-3′), 3.68 (H, *dd*, $J = 6$, 12 Hz, H-6′a), 3.89 (3H, *s*, -OMe), 3.92 (H, *dd*, $J = 2$, 12 Hz, H-6′b), 3.97 (H, *s*, H-7), 4.69 (H, *d*, $J = 8$ Hz, H-1′), 5.28 (H, *br t*, $J = 5$ Hz, H-7), 5.29 (H, *d*, $J = 5$ Hz, H-1), 6.38 (H, *d*, $J = 16$ Hz, H-8″), 6.81 (H, *d*, $J = 8$ Hz, H-5″), 7.08 (H, *dd*, $J = 2$, 8 Hz, H-6″), 7.21 (H, *d*, $J = 2$ Hz, H-2″), 7.46 (H, *d*, $J = 1$ Hz, H-2), 7.61 (H, *d*, $J = 16$ Hz, H-7″); ^{13}C NMR (CD_3OD): Table 1; HR-FAB-MS (negative centroid) *m/z*: 551.1793 $[M-H]^-$ ($C_{26}H_{31}O_{13}$ requires 551.1765).

7-O-Z-*Feruloylloganic acid* (**3**). Amorphous powder, $[\alpha]_D^{25}$ −49.4° (MeOH, *c* 0.57). UV λ_{max}^{MeOH} nm (log ε): 224 (4.21)sh, 232 (4.23), 302 (3.94)sh, 324 (4.05); ^{1}H NMR (CD_3OD): δ 1.03 (3H, *d*, $J = 7$ Hz, H_3-10), 1.80 (H, *ddd*, $J = 5$, 8, 14 Hz, H-6β), 1.98 (H, *dt*, $J = 5$, 8 Hz, H-9), 2.15 (H, *m*, H-8), 2.23 (H, *ddd*, $J = 1$, 8, 13 Hz, H-6α), 3.06 (H, *br q*, $J = 8$ Hz, H-5), 3.21 (H, *dd*, $J = 8$, 9 Hz, H-2′), 3.38 (H, *t*, $J = 9$ Hz, H-3′), 3.06 (H, *br q*, $J = 7$ Hz, H-8), 3.67 (H, *dd*, $J = 6$, 12 Hz, H-6′a), 3.87 (3H, *s*, -OMe), 3.90 (H, *dd*, $J = 2$, 12 Hz, H-6′b), 5.21 (H, *br t*, $J = 5$ Hz, H-7), 5.26 (H, *d*, $J = 5$ Hz, H-1), 4.66 (H, *d*, $J = 8$ Hz, H-1′), 5.80 (H, *d*, $J = 13$ Hz, H-8″), 6.77 (H, *d*, $J = 8$ Hz, H-5″), 6.88 (H, *d*, $J = 13$ Hz, H-7″), 7.08 (H, *dd*, $J = 2$, 8 Hz, H-6″), 7.43 (H, *d*, $J = 1$ Hz, H-3), 7.68 (H, *d*, $J = 2$ Hz, H-2″); ^{13}C NMR (CD_3OD): Table 1; HR-FAB-MS (negative centroid) *m/z*: 551.1756 $[M-H]^-$ ($C_{26}H_{31}O_{13}$ requires 551.1765).

Acetylation of alangiplatanoside (**1**). About 2 mg of **1** was acetylated with 100 μl each of Ac_2O and pyridine at 50° for 18 hr. The reagents were evapd off under a stream of N_2, followed by purification by prep.

TLC [silica gel, precoated plates (10 × 13 cm), 0.25 mm thickness (Merck), developed with C_6H_6–Me_2CO (4:1) and eluted with $CHCl_3$–MeOH (9:1)] to give an octaacetate (**1a**). ^1H NMR ($CDCl_3$): δ 1.97 (s) and 1.98 (1) (3H, *s*), 2.00 (3H, *s*), 2.022 (3H, *s*), 2.024 (3H, *s*), 2.04 (1), 2.04 (*s*) (3H, *s*), 2.07 (3H, *s*), 2.090 (3H, *s*), 2.091 (3H, *s*), rotation of the sugar moiety seems to be restricted, *s* in parentheses denotes signals from the minor rotamer and one from the major rotamer; EIMS *m/z* (rel. int.): 990 (5.9) $[M]^+$, 930 (0.6) $[M - AcOH]^+$, 547 (61) $[Api(OAc)_3Glu(OAc)_3$ oxonium ion$]^+$, 444 (42) [aglycone + H]$^+$, 418 (8), 259 (100) $[Api(OAc)_3$ oxonium ion$]^+$, 169 (36), 157 (22), 139 (100), 129 (31), 109 (26), 97 (46), 43 (100); FABMS (*m*-nitrobenzyl alcohol) *m/z*: 1013 $[M + Na]^+$ (+NaI), 1029 $[M + K]^+$ (+KI).

GC analysis of the sugar portion of **1**. A few mg of **1** was treated with 5% HCl in MeOH at 95° for 3 hr. The reaction mixt. was neutralized with Ag_2CO_3 and then filtered. The filtrate was concd and the residue was trimethylsilylated with a few drops of TMS–imidazole for 15 min at 60°. The reaction mixt. was partitioned between *n*-hexane (2 ml) and H_2O (2 ml), and the concd organic layer was subjected to GC analysis. GC: Shimadzu GC-8A gas chromatograph with FID, column: Shimadzu CPB-20, 0.22 mm × 25 m, layer thickness: 0.25 μm; temp.: 160°; carrier gas: N_2 at 1.5 kg cm^{-2}. Standard sugars, apiose: 2.71, 2.84, 2.96 and 3.15 min; glucose: 8.18 and 8.87 min (the standard apiose was available from a previous experiment [8]). Compound **1**: 2.73, 2.84, 2.98 and 3.15 min (apiose), and 8.16 and 8.84 min (glucose).

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