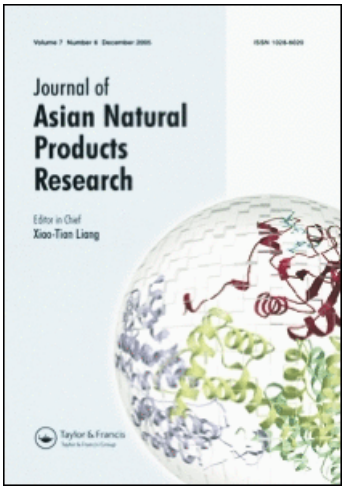

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ORIGINAL ARTICLE

Chemical constituents from the leaves of *Aglaia perviridis*

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A new cinnamic acid-derived bisamide **1** and a new oplopanone-type sesquiterpenoid diglycoside **2**, together with 11 known compounds, were isolated from the 95% ethanolic extract of the leaves of *Aglaia perviridis*. Their structures were elucidated by chemical and spectroscopic methods.

Keywords: *Aglaia perviridis* Hiern; 4-hydroxypyramidatine; oplopanone 10-*O*-β-D-(5-*O*-syringoyl)-apiofuranosyl-(1 → 2)-β-D-glucopyranoside

1. Introduction

The genus *Aglaia* belongs to the family Meliaceae, which is distributed in South China, India, Malaysia, Indonesia, and parts of the Western Pacific region. Extracts of these plants have been used for the treatment of fever, inflammation, and abdominal tumors and as bactericides and insecticides [1]. Previous phytochemical studies on the genus *Aglaia* have revealed the presence of a variety of compounds with interesting biological activities, including rocaglamides, aglains, bisamides, triterpenoids, lignans, and steroids [2]. In continuation of our investigation on the chemistry of the *Aglaia* plants [3,4], we undertook a chemical constituent study on the 95% ethanolic extract of the leaves of *Aglaia perviridis* Hiern, which led to the isolation of a new cinnamic acid-derived bisamide **1** and a new sesquiterpenoid diglycoside **2**, together with 11 known compounds, including three 3,4-secodammarane triterpenoids: aglinin A [5], shoric acid, and eichlerianic acid [6]; two C_{27} nortriterpenoids: eichlerialactone [7] and cabraleahydroxylactone [8]; two pregnane-type steroids: 2β,3β-dihydroxy-5α-pregn-17(*Z*)-en-16-one and 2β,3β-dihydroxy-5α-pregn-17(*E*)-en-16-one [9]; two alkaloids: pyramidatine [10] and piperine [11]; one lignan: (+)-eudesmin [12]; and one sterol: 7α-hydroxysitosterol [13]. Eichlerialactone was first reported from this genus, and the other compounds were obtained from this plant for the first time. Herein, we report the isolation and structural elucidation of **1** and **2**.

2. Results and discussion

Compound **1**, obtained as a white amorphous powder, had quasi-molecular ion peaks at *m/z* 361 ($[M+Na]^+$) and *m/z* 337

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($[M-H]^-$) in the positive and negative ESI-MS, respectively, in accord with the molecular formula $C_{20}H_{22}N_2O_3$, which was further confirmed by HR-ESI-MS (found $[M+Na]^+$ 361.1523, $C_{20}H_{22}N_2O_3Na$ requires 361.1528). The ^1H NMR spectrum of **1** showed signals for two aromatic rings, of one 1,4-disubstituted at δ_H 7.81 (2H, d, $J = 8.4$ Hz) and 6.87 (2H, d, $J = 8.4$ Hz), and of one mono-substituted at δ_H 7.57 (2H, br d, $J = 8.4$ Hz), 7.40 (2H, br t, $J = 7.6$ Hz), and 7.38 (1H, br t, $J = 6.6$ Hz), one pair of conjugated *E*-double bond at δ_H 7.54 and 6.70 (each 1H, d, $J = 15.6$ Hz), and a 1,4-butanediamine fragment at δ_H 7.84 and 7.70 (each 1H, br s), 3.41 (2H, br q, $J = 6.1$ Hz), 3.36 (2H, br q, $J = 6.1$ Hz), and 1.64 (4H, *qui*-like, $J = 6.0$ Hz), indicating a cinnamic acid-derived bisamide [10].

The ^{13}C NMR spectral data of **1** were similar to those of pyramidatine [10], except for the signals for a *p*-hydroxybenzoic amide unit instead of those for the benzoic amide fragment of the latter. HMBC and HMQC experiments (Figure 1) confirmed the fragment of 1,4-butanediamine to be connected with the cinnamic acid amide and *p*-hydroxybenzoic amide through two terminal N atoms. Therefore, the structure of **1** was elucidated to be 4-hydroxypyramidatine.

Compound **2** was obtained as a white amorphous powder, and it had the molecular formula $C_{35}H_{52}O_{15}$ deduced from the quasi-molecular ion peak at *m/z* 735.3209 ($[M+Na]^+$) in the HR-ESI-MS. Under acid hydrolysis, **2** gave D-glucose and D-apiose as the sugar moiety. The ^1H and ^{13}C NMR spectra (Table 1) showed signals for a syringoyl at δ_H 7.41 (2H, s) and 3.92 (6H, s) and δ_C 166.3 (s), 148.1 (2C, s), 141.7 (s), 120.6 (s), 107.8 (2C, d), 56.4 (2C, q), a β-apiofuranosyl at δ_H 5.58 (1H, br s) and δ_C 109.3 (d), 78.2 (s), 78.1 (d), 75.0 (t), 69.7 (t), one β-glucopyranosyl groups at δ_H 4.63 (d, $J = 7.6$ Hz) and δ_C 96.0 (d), 78.7 (d), 76.7 (d), 76.5 (d), 71.7 (d), 62.5 (t), and a sesquiternoid segment (four methyls, four methylenes, five methines, and two quaternary carbons). The aglycone was characterized

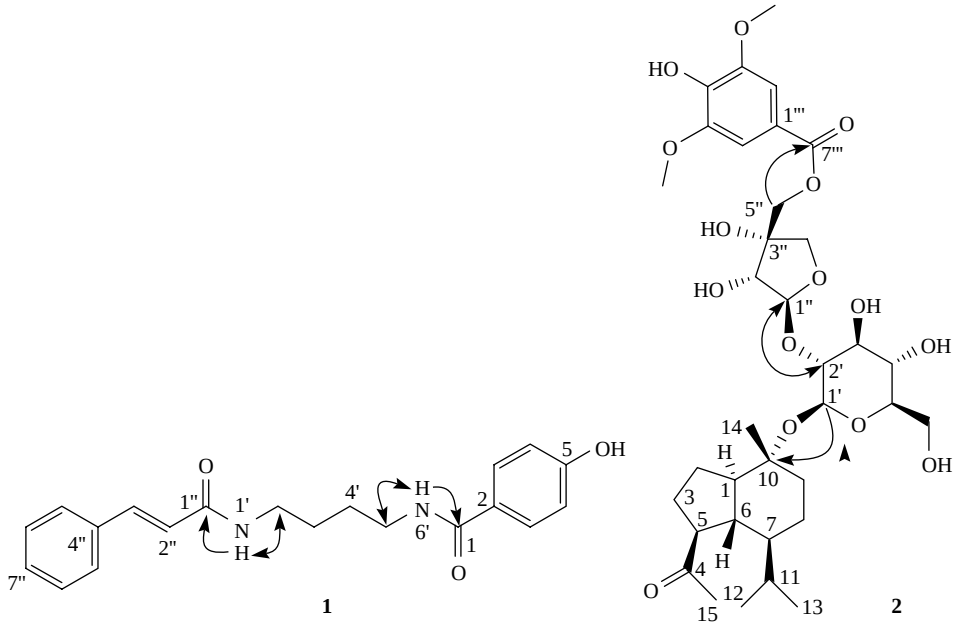

Figure 1. The structures and the selective HMBC correlations (H → C) of **1** and **2**.

Table 1. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectral data of **2** (in acetone-d_6).

Site	δ_H	δ_C
1	1.50 (m)	55.9
2	α: 1.25 (m); β: 1.81 (m)	26.0
3	α: 1.37 (m); β: 1.80 (m)	29.0
4	–	210.6
5	2.15 (m)	54.8
6	1.71 (m)	45.9
7	0.95 (br q, 12.1)	49.2
8	α: 0.90 (m); β: 1.50 (m)	22.8
9	α: 1.34 (m); β: 1.99 (m)	38.2
10	–	79.7
11	1.28 (m)	29.8
12	0.86 (3H, d, 7.0)	21.8
13	0.59 (3H, d, 7.0)	15.5
14	1.21 (3H, s)	18.4
15	1.96 (3H, s)	29.2
1′	4.63 (d, 7.6)	96.0
2′	3.39 (dd, 9.2, 7.8)	76.7
3′	3.58 (dd, 9.1, 8.8)	78.7
4′	3.33 (dd, 9.5, 8.4)	71.7
5′	3.27 (ddd, 9.5, 5.4, 2.6)	76.5
6′	3.79 (dd, 11.2, 2.6); 3.62 (dd, 11.2, 5.4)	62.5
1″	5.58 (br s)	109.3
2″	3.99 (s)	78.1
3″	–	78.2
4″	4.31 (d, 10.0); 3.94 (d, 10.0)	75.0
5″	4.45 (d, 11.0); 4.31 (d, 11.0)	69.7
1‴	–	120.6
2‴/6‴	7.41 (2H, s)	107.8
3‴/5‴	–	148.1
4‴	–	141.7
7‴	–	166.3
OMe	3.92 (6H, s)	56.4

with an acetyl at δ_C 210.6 (s), 29.2 (q) and δ_H 1.96 (3H, s) and an isopropyl group at δ_H 0.59 (d, $J = 7.0$ Hz) and 0.86 (d, $J = 7.0$ Hz), indicative of an oplopanone-type sesquiterpenoid [14]. The ^{13}C NMR data for the aglycone were nearly superposed with those of (−)-oplopan-4-one-10-α-*O*-β-glucose [15], demonstrating oplopanone as the aglycone moiety of **2**. The NOESY spectrum revealed the NOE cross-peaks of H-1/H-5, H-7, and H-8α, 14-Me/H-2β, H-6, and H-9β, indicating that **2** had the same configurations of H-1α, H-5α, H-6β, H-7α, and 14-Meβ as those of (−)-oplopan-4-one-10-α-*O*-β-glucose.

The glycone moiety was determined as β-D-(5-*O*-syringoyl)-apiofuranosyl-(1 → 2)-β-D-glucopyranosyl based on the ^{13}C NMR spectral data comparison with those of albibrissinoside A [16], which has the same sugar moiety, as well as the HMBC correlations (Figure 1). Furthermore, the HMBC correlations between C-10 and H-1′ demonstrated the glycone unit to be attached on C-10. Consequently, the structure of **2** was finally determined to be oplopanone 10-*O*-β-D-(5-*O*-syringoyl)-apiofuranosyl-(1 → 2)-β-D-glucopyranoside.

3. Experimental

3.1 General experimental procedures

Optical rotations were determined on a Perkin-Elmer 341 polarimeter. The IR spectra were recorded on a Nicolet-Magna-750-FTIR spectrometer. The NMR spectra were taken on a Bruker AV-400 spectrometer using TMS as an internal standard. ESI-MS spectra were measured on a Bruker Esquire 3000 plus mass spectrometer. The HR-ESI-MS spectra were obtained on a Finnigan LC QDECA mass spectrometer. Silica gel (200–300 mesh) or silica gel H (Qingdao Haiyang, Co., Qingdao, China), Sephadex LH-20 (Pharmacia Biotech AB, Uppsala, Sweden) were used for column chromatography (CC), and silica gel $HSGF_{254}$ (Yantai Jiangyou Guijiao Kaifa Co., Yantai, China) was used for TLC.

3.2 Plant material

The leaves of *A. perviridis* (Meliaceae) were collected in Xishuangbanna County, Yunnan Province, China, in July 2006. The plant was identified by Prof. Jing-Yun Cui of Xishuangbanna Tropical Botanical Garden, CAS. A voucher specimen (No. 20061058) is deposited at the Herbarium of Shanghai Institute of Materia Medica.

3.3 Extraction and isolation

The dry leaves of *A. perviridis* (5 kg) were extracted with 20 liters of 95% EtOH at room temperature for three times. The concentrated extract was partitioned between H_2O and petroleum ether, $CHCl_3$, EtOAc, and BuOH, respectively. The $CHCl_3$ fraction (142 g) was subjected to chromatography of a silica gel column (i.d. 10×80 cm) with the gradient $CHCl_3$–Me_2CO (1:0, 25:1, 10:1, 5:1, 2:1, 0:1) as eluents to give six fractions (A–F). Fraction A yielded solids, which was further purified by silica gel CC ($CHCl_3$–MeOH, 30:1) to afford 7α-hydroxysitosterol (100 mg). Fraction B was subjected to silica gel CC ($CHCl_3$–Me_2CO, 15:1) to yield fractions B1–B5. Fraction B2 furnished (+)-eudesmin (40 mg) after purification of silica gel CC ($CHCl_3$–MeOH, 25:1). Fraction C was subjected to silica gel CC ($CHCl_3$–Me_2CO, 10:1) to obtain fractions C1–C6. Fraction C5 gave piperine (40 mg) after purification of silica gel CC ($CHCl_3$–Me_2CO, 5:1). Fraction D was separated into fractions D1–D5 through a silica gel column ($CHCl_3$–MeOH, 15:1). Fractions D4 and D5 furnished aglinin A (1.6 g) and eichlerialactone (1.0 g), respectively, by methods of recrystallization. Fraction E was further isolated by silica gel CC ($CHCl_3$–MeOH, 15:1) to provide fractions E1–E6. Shoric acid (1.5 g) and eichlerianic acid (1.3 g) were obtained as crystals from fractions E3 and E4, respectively. Fraction E5 was purified by silica gel CC ($CHCl_3$–MeOH, 10:1) to afford cabraleahydroxylactone (60 mg). Fraction F was subjected to silica gel CC ($CHCl_3$–MeOH, 10:1) to gain fractions F1–F6. Fraction F4 yielded mixed solids, which were further isolated by silica gel CC ($CHCl_3$–MeOH, 10:1) to obtain 2β,3β-dihydroxy-5α-pregn-17(*Z*)-en-16-one (7 mg) and 2β,3β-dihydroxy-5α-pregn-17(*E*)-en-16-one (8 mg). The EtOAc-soluble fraction (60 g) was separated into fractions I–IV by silica gel CC ($CHCl_3$–MeOH, 30:1, 20:1, 10:1, and 5:1). Fraction I gave pyramidatine (1.5 g) as crystals. Fraction II was subjected to silica gel CC ($CHCl_3$–MeOH, 15:1) to yield fractions II.1–II.4. Compound **1** (15 mg) was isolated from fraction II.3 through CC (Sephadex LH-20, MeOH). Compound **2** (12 mg) was acquired from fraction III after purification of a silica gel column ($CHCl_3$–MeOH, 8:1), and then of a Sephadex LH-20 column (MeOH).

*3.3.1 4-Hydroxypyramidatine (**1**)*

White amorphous powder. UV (MeOH) λ_{max} (log ε): 202 (4.87), 267 (4.72) nm. IR ν_{max}: 3292, 1701, 1655, 1626, 1540.9, 1508, 1248, 848, 768 cm^{-1}. ^1H NMR spectral data (acetone-d_6, 400 MHz): δ 7.84 (1H, br s, H-6′), 7.81 (2H, d, $J = 8.4$ Hz, H-3 and H-7), 7.70 (1H, br s, H-1′), 7.57 (2H, br d, $J = 8.4$ Hz, H-5″ and H-9″), 7.54 (1H, d, $J = 15.6$ Hz, H-3″), 7.40 (2H, br t, $J = 7.6$ Hz, H-6″ and H-8″), 7.38 (1H, br t, $J = 6.6$ Hz, H-7″), 6.87 (2H, d, $J = 8.4$ Hz, H-4 and H-6), 6.70 (1H, d, $J = 15.6$ Hz, H-2″), 3.41 (2H, br t, $J = 6.1$ Hz, H_2-5′), 3.36 (2H, br t, $J = 6.1$ Hz, H_2-2′), 1.64 (4H, *qui*-like, $J = 6.0$ Hz, H_2-3′ and H_2-4′). ^{13}C NMR (acetone-d_6, 100 MHz): δ 167.0 (C-1″), 165.9 (C-1), 160.7 (C-5), 139.7 (C-3″), 135.9 (C-4″), 129.8 (C-7″), 129.5 (C-3 and C-7), 129.3 (C-6″ and C-8″), 128.1 (C-5″ and C-9″), 126.5 (C-2), 122.5 (C-2″), 115.3 (C-4 and C-6), 39.4 (C-5′), 39.2 (C-2′), 27.5 (C-3′), 27.4 (C-4′). ESI-MS (positive or negative): *m/z* 361.1 $[M+Na]^+$, 699.3 $[2M+Na]^+$, 337.1 $[M-H]^-$; HR-ESI-MS: *m/z* 361.1523 $[M+Na]^+$ (calcd for $C_{20}H_{22}N_2O_3Na$, 361.1528).

*3.3.2 Oplopanone 10-O-β-D-(5-O-syringoyl)apiofuranosyl-(1 → 2)-β-D-glucopyranoside (**2**)*

White amorphous powder. $[\alpha]_D^{25}$: −13.2 ($c = 0.600$, MeOH). UV (MeOH) λ_{max} (log ε): 219 (3.95), 279 (4.66) nm. IR ν_{max}:

3408, 1709, 1610, 1516, 1464, 1221 cm^{-1}. ^1H and ^{13}C NMR: see Table 1. ESI-MS (positive or negative): *m/z* 735 $[M+Na]^+$, 1447 $[2M+Na]^+$, 711 $[M-H]^-$; HR-ESI-MS: *m/z* 735.3209 $[M+Na]^+$ (calcd for $C_{35}H_{52}O_{15}Na$, 735.3204).

3.3.3 *Acid hydrolysis of* **2**

Two milligrams of **2** were dissolved in 2 ml of 2 M HCl–dioxane (1:1), and then the solution was refluxed for 2 h. After cooling, the solution was neutralized with $NaHCO_3$, and then filtered to remove the solid. The filtrate was subjected to CC (Sephadex LH-20, MeOH–H_2O, 1:1) to afford a sugar fraction. This sugar fraction and standard D-glucose and D-apiose (Sigma, St Louis, MO, USA) were each treated with L-cysteine methyl ester hydrochloride (2 mg) in pyridine (1 ml) at 60°C for 1 h. Then, the solution was treated with *N*,*O*-bis(trimethylsilyl)trifluoroacetamide (0.02 ml) at 60°C for 1 h. Subsequently, the supernatant was subjected to GC analysis (230°C, flow rate 15 ml/min; Supelco, Bellefonte, PA, USA). D-Glucose (t_R 24.2 min) and D-apiose (t_R 14.2 min) were detected.

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