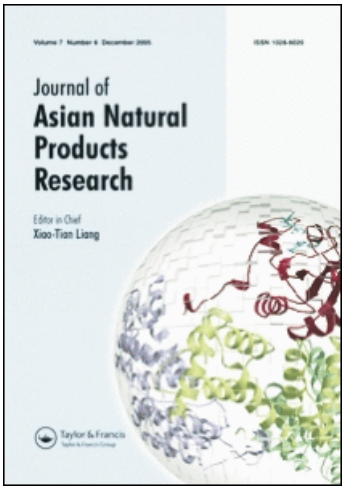

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Two new pregnanes from *Aglaia perviridis* Hiern

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Two new pregnanes, 2α,3α,20-trihydroxy-16β-acetoxy-20(*R*)-pregnane (**1**) and 2α,3α,15β-trihydroxy-16β-acetoxy-pregnane-20(*R*)-methacrylate (**2**), along with five known compounds, were isolated from the ethanolic extract of the twigs of *Aglaia perviridis* Hiern using chromatographic methods. The structures of **1** and **2** were elucidated on the basis of spectral data.

Keywords: *Aglaia perviridis* Hiern; pregnane; 2α,3α,20-trihydroxy-16β-acetoxy-20(*R*)-pregnane; 2α,3α,15β-trihydroxy-16β-acetoxy-pregnane-20(*R*)-methacrylate

1. Introduction

Previous phytochemistry investigations on the genus *Aglaia* have revealed the presence of a variety of compounds with interesting biological activities, including rocaglamides, aglains, bisamides, triterpenes, lignans and steroids.[1–5] In continuation of our research on the chemistry of the Meliaceae species, we undertook a chemical study on the ethanolic extract of the twigs of *Aglaia perviridis* Hiern, mainly distributed in South China and India.[6] Two new pregnanes, 2α,3α,20-trihydroxy-16β-acetoxy-20(*R*)-pregnane (**1**), 2α,3α,15β-trihydroxy-16β-acetoxy-pregnane-20(*R*)-methacrylate (**2**), together with five known compounds, (*E*)-aglawone (**3**),[7] (*E*)-aglawone-3-one (**4**),[8] lansisterone E (**5**),[9] 2β,3β,4β-trihydroxypregnan-16-one (**6**)[10] and 2,19-oxymeliavosin (**7**)[10] were obtained from this species. Their structures were elucidated by spectroscopic measurements including ESI-MS, IR, 1D and 2D NMR spectra.

2. Results and discussion

Compound **1** was found to have the molecular formula $C_{23}H_{38}O_5$ deduced by HR-ESI-MS quasimolecular ion peak at *m/z* 417.2617 ($[M + Na]^+$). The ^1H and ^{13}C NMR spectral data of **1** were almost superposed with those of 2α,3α,16β,20(*R*)-tetrahydroxy-pregnane (**8**),[11] except for an additional acetoxyl group (δ_C 172.7 and 21.6, δ_H 1.98) and the downfield shift of $\delta_{C\text{-}16}$ (+5.4 ppm) (Table 1), suggesting an C-16-acetoxylated analog of **8**. This assumption was further confirmed by the HMBC cross-peak of δ_C 172.7 (s, CH_3COO) with δ_H 5.07 (1H, dt, $J = 7.8$, 4.2 Hz, H-16). Consequently, **1** was established to be 2α,3α,20-trihydroxy-16β-acetoxy-20(*R*)-pregnane.

Compound **2** possessed the molecular formula $C_{27}H_{42}O_7$ as evidenced by HR-ESI-MS (*m/z* 501.2859, $[M + Na]^+$). The IR spectrum showed the absorption bands for hydroxyl groups (3420 cm^{-1}), carbonyl group (1716 cm^{-1}) and double bonds (1637 cm^{-1}).

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Table 1. ^{1}H and ^{13}C NMR spectral data of **1** and **2**.[a,b,c]

	δ_C		δ_H	
	1	**2**	**1**	**2**
1	42.1 t	42.0 t	1.63 (1H, m) 1.28 (1H, m)	1.87–1.93 (1H, m) 2.07 (1H, m)
2	70.4 d	69.0 d	3.65 (1H, ddd, 12.1, 4.3, 3.3)	4.17 (1H, ddd, 11.9, 3.9, 3.3)
3	71.0 d	69.8 d	3.87 (1H, brs)	4.47 (1H, brs)
4	36.2 t	35.6 t	1.46–1.52 (2H, m)	1.87–1.93 (1H, m) 1.65 (1H, m)
5	40.0 d	38.8 d	1.53 (1H, m)	2.09 (1H, m)
6	29.3 t	28.1 t	1.25 (2H, m)	1.43 (2H, m)
7	33.6 t	31.6 t	1.65 (1H, m) 0.93 (1H, m)	1.96 (1H, m) 1.15 (1H, m)
8	36.1 d	31.1 d	1.46–1.52 (1H, m)	1.99 (1H, m)
9	56.5 d	55.1 d	0.80 (1H, m)	1.02 (1H, m)
10	38.4 s	37.3 s		
11	22.2 t	20.8 t	1.55 (1H, m) 1.33 (1H, dd, 12.6, 3.0)	2.15 (1H, m) 1.65 (1H, m)
12	41.3 t	40.8 t	2.16 (1H, dt, 12.6, 3.0) 1.17 (1H, td, 12.6, 3.0)	2.05 (1H, m) 1.31 (1H, m)
13	44.5 s	43.1 s		
14	55.6 d	56.8 d	0.99 (1H, m)	1.19 (1H, m)
15	36.9 t	71.2 d	2.34 (1H, ddd, 13.5, 7.8, 7.3) 1.10 (1H, td, 13.5, 4.2)	4.74 (1H, dd, 13.8, 7.2)
16	77.2 d	74.2 d	5.07 (1H, dt, 7.8, 4.2)	5.50 (1H, t, 6.0)
17	63.4 d	60.5 d	1.41 (1H, dd, 10.1, 7.8)	1.83 (1H, dd, 10.8, 7.8)
18	14.1 q	15.9 q	0.96 (3H, s)	1.40 (3H, s)
19	13.4 q	12.7 q	0.84 (3H, s)	0.92 (3H, s)
20	67.0 d	71.2 d	4.00 (1H, dq, 10.8, 5.9)	6.01 (1H, dq, 10.8, 5.9)
21	23.9 q	20.2 q	1.12 (3H, d, 5.9)	1.72 (3H, d, 5.9)
1′		166.7 s		
2′		137.5 s		
3′		125.5 t		6.41 (1H, brs) 5.82 (1H, brs)
4′		18.6 q		2.16 (3H, brs)
CH_3COO	172.7 s	171.2 s		
CH_3COO	21.6 q	21.0 q	1.98 (3H, s)	2.24 (3H, s)

[a]The ^{1}H and ^{13}C NMR spectra were measured in 400 and 100 MHz, respectively, J in Hz and δ in ppm.
[b]**1** in CD_3OD and **2** in pyridine-d_5.
[c]Multiplicities were overlapped and assigned based on the HMQC and ^{1}H–^{1}H COSY experiments.

The ^{13}C NMR and DEPT spectra displayed signals for 27 carbons, including 5 methyl groups, 7 methylenes, 10 methines, 5 quaternary carbons and 1 methacrylate group (δ_C 18.6, 125.5, 137.5, 166.7) and 1 acetoxyl group (δ_C 21.0, 171.2) (Table 1), indicating an analog of **1**. Comparison of the ^{1}H and ^{13}C NMR spectra of **2** with those of **1** showed that the most important differences lie in an additional methacryloxyl group and an oxygenated CH in **2** instead of one CH_2 in **1**, suggesting **2** to be an analog of **1** substituted by a hydroxyl group and a methacryloyl group. The hydroxyl group was assigned by the following analyses of the 2D NMR spectra: starting from diagnostic 21-Me, the ^{1}H–^{1}H COSY and HMQC spectra showed the D-ring linkage clearly (Figure 1), proving the hydroxyl group to be located on C-15. The obvious NOE correlations of H-15 with H-14, H-16 and H-17 (Figure 1) indicated the β-orientation of 15-OH. The methacryloxyl group was positioned on C-20 by HMBC correlations of H-20/C-1′ and H-20/C-21, and H-4′/C-3′, C-2′, and C-1′. Furthermore, 16-acetoxyl group was also confirmed by the correlation of H-16/C-OAc in the HMBC spectrum. Therefore, **2** was elucidated to be 2α,3α,15β-trihydroxy-16β-acetoxy-pregnane-20(*R*)-methacrylate, i.e. 15β-hydroxy-16β-acetoxyl-azedarachol.[12]

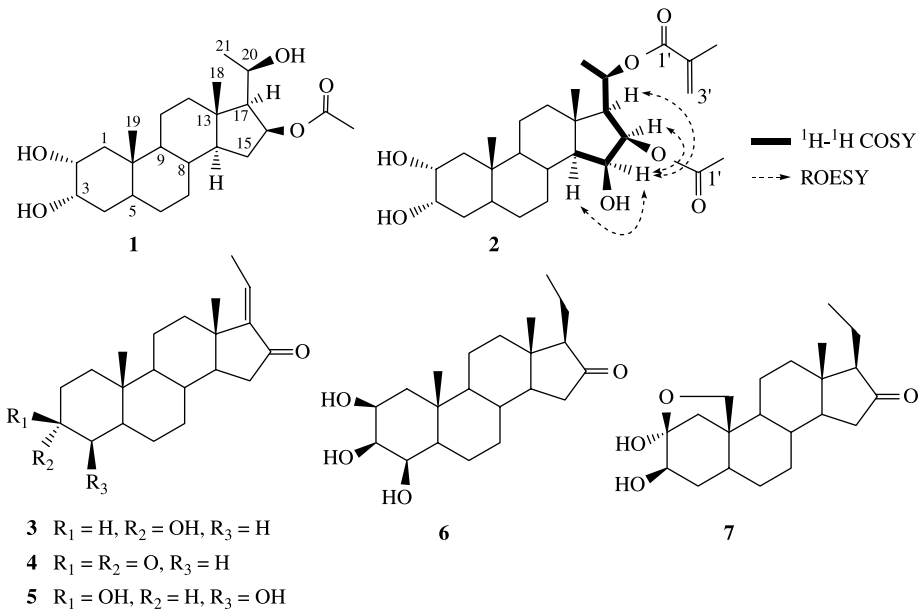

Figure 1. Key ^{1}H–^{1}H COSY and ROESY correlations for **2** and structures of **1**–**7**.

The known compounds were identified to be (*E*)-aglawone (**3**),[7] (*E*)-aglawone-3-one (**4**),[8] lansisterone E (**5**),[9] 2β,3β,4β-trihydroxypregnan-16-one (**6**)[10] and 2,19-oxymeliavosin (**7**)[10] on the basis of optical rotation, ^{1}H, ^{13}C NMR and MS spectra, as well as by comparison of their spectral data with those of reported previously. Compounds **3**–**7** were obtained from this species for the first time.

3. Experimental

3.1 General experimental procedures

Optical rotations were determined on a DIP digital polarimeter. The IR spectra were recorded on a Nicolet 750 instrument. The NMR spectra were taken on a Brucker AM-400 spectrometer using TMS as an internal standard. ESI-MS spectra were measured on an LCQ Deca mass spectrometer. The HR-ESI-MS spectra were obtained on an Apex mass spectrometer.

3.2 Plant material

The twigs of *A. perviridis* were collected in Xishuangbanna County, Yunnan Province, China, in July 2006. The plants were identified by Professor Jing-Yun Cui (Xishuangbanna Tropic Botanic Garden, Chinese Academy of Sciences, Yunnan, China). A voucher specimen was deposited at the State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, China.

3.3 Extraction and isolation

Air-dried twigs (46 kg) were crushed and extracted with 95% EtOH at reflux to yield an EtOH extract. After removal of the EtOH *in vacuo*, the viscous concentration was partitioned between H_2O and petroleum ether, $CHCl_3$ and *n*-BuOH, respectively. The $CHCl_3$ fraction (151 g) was chromatographed on a pre-packed Si gel column, using a gradient of $CHCl_3$–Me_2CO (from 1:0 to 1:1) to give 13 fractions (Fr. 1–Fr. 13) according to the differences in composition monitored by TLC (Si gel GF_{254}). From Fr. 3 (9 g), **4** (23 mg) was obtained by repeated chromatography using gradient elution with petroleum ether–EtOAc. Fr. 4 (10.5 g) and Fr. 7 (9.7 g) were subjected to silica gel column chromatography

(CC) using gradient elution with petroleum ether–EtOAc, and then recrystallized in acetone to obtain **3** (64 mg) from Fr. 4 and **5** (64 mg) from Fr. 7, respectively. Fr. 9 (2.5 g) was purified by repeated CC silica gel using petroleum ether–EtOAc (6:4) as eluent to give **2** (48 mg) and **7** (168 mg). Fr. 11 (4.3 g) was chromatographed over silica gel, eluted by petroleum ether–Me_2CO, further purified by RP-18 gel, eluted with MeOH–H_2O (from 4:6 to 9:1) to obtain **1** (17 mg) and **6** (14 mg).

*3.3.1 2α,3α,20-Trihydroxy-16β-acetoxy-20(*R*)-pregnane (**1**)*

White powder; $[\alpha]_D^{25}$ + 70.9 (*c* 0.385, MeOH); IR (KBr) ν_{max}: 3427, 2928, 2856, 1712, 1639, 1454, 1379, 1267, 1047 cm^{-1}; ^1H and ^{13}C NMR spectral data (Table 1); ESI-MS: *m/z* 417 $[M + Na]^+$, 811 $[2M + Na]^+$; HR-ESI-MS: *m/z* 417.2617 $[M + Na]^+$ (calcd for $C_{23}H_{38}O_5Na$, 417.2617).

*3.3.2 2α,3α,15β-Trihydroxy-16β-acetoxy-pregnane-20(*R*)-methacrylate (**2**)*

White powder; $[\alpha]_D^{25}$ − 10 (*c* 0.250, MeOH); IR (KBr) ν_{max}: 3402, 2950, 2922, 2854, 1716, 1637, 1450, 1379, 1261, 1174, 1043, 937 cm^{-1}; ^1H and ^{13}C NMR spectral data (Table 1); ESI-MS: *m/z* 501 $[M + Na]^+$, 979 $[2M + Na]^+$; HR-ESI-MS: *m/z* 501.2859 $[M + Na]^+$ (calcd for $C_{27}H_{42}O_7Na$, 501.2828).

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