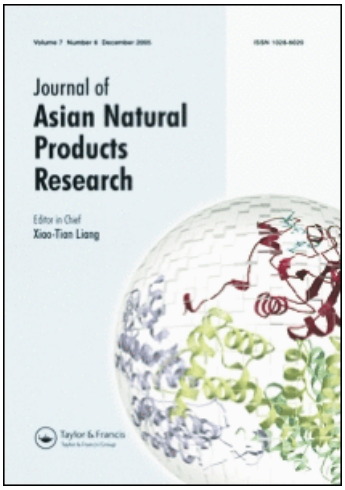

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Scyphiphin D, a new iridoid glucoside dimer from *Scyphiphora hydrophyllacea*

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From the aerial parts of *Scyphiphora hydrophyllacea* Gaertn. F., a new iridoid glucoside dimer scyphiphin D (**1**) and a known iridoid glucoside geniposidic acid (**2**) were isolated. The structure of this new compound was determined on the basis of HR-FAB-MS, IR, ^{1}H and ^{13}C NMR (DEPT), and 2D NMR (HMQC, HMBC, COSY, ROESY) spectral data.

Keywords: scyphiphin D; iridoid glucoside dimer; *Scyphiphora hydrophyllacea*; mangrove plant

1. Introduction

Mangrove plants are groups of trees and shrubs growing along seashores in tropical and subtropical areas subjected to tidal influences and having specially adapted physiological metabolic pathways. Consequently, mangrove plants contain plenty of new and bioactive secondary metabolites [1–3]. *Scyphiphora hydrophyllacea* Gaertn. F. (Rubiaceae), one of the mangrove plants, is distributed from South to Southeast Asia, Caroline Islands, Australia, and New Caledonia [4]. Previously, phytochemical studies showed that iridoids were characteristic constituents of *S. hydrophyllacea* [5–9]. In continuation of our study on *S. hydrophyllacea* collected in the mangrove forest in Hainan Island, a new iridoid glucoside dimer scyphiphin D (**1**) and a known iridoid glucoside geniposidic acid (**2**) (Figure 1) were isolated from the 95% ethanol extract of the aerial parts of this plant. In this paper, we present the isolation and structural characterization of this new iridoid glucoside dimer on the basis of the interpretation of spectral data, including 1D and 2D NMR data.

2. Results and discussion

Compound **1** was obtained as a white amorphous powder. The molecular formula of **1** was established as $C_{32}H_{42}O_{19}$ with 12 degrees of unsaturation according to the high-resolution ESI-MS data at *m/z* 753.2224 $[M + Na]^+$, which was also supported by ^{13}C NMR and DEPT spectral data. Its IR spectrum showed the presence of hydroxyl (3423 cm^{-1}), ester (1691 cm^{-1}), and olefinic (1631 cm^{-1}) groups. The ^{13}C NMR and DEPT spectra of **1** presented 32 carbon signals including 6 methylenes (δ 39.8, 40.0, 61.5, 62.7, 62.8, 63.4), 20 methines (δ 36.4, 36.6, 47.1, 47.7, 71.5, 71.6, 74.8, 74.9, 77.9, 78.0, 78.4, 78.4, 98.3, 98.4, 100.4, 100.6, 128.5, 131.1, 153.3, 153.7), and 6 quaternary carbons (δ 112.6,

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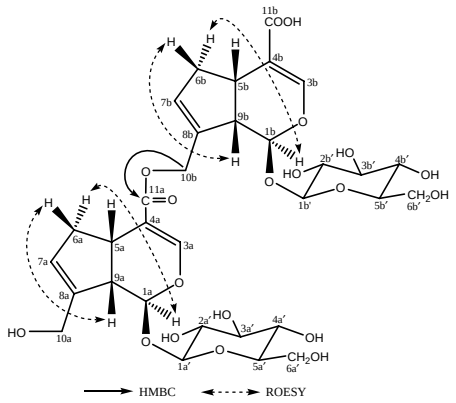

Figure 1. Key HMBC and ROESY correlations of compound **1**.

112.6, 139.8, 144.7, 168.9, 170.9). The ^{1}H NMR spectrum of **1** showed two iridoid characteristic proton signals at δ_H 5.18 (1H, d, $J = 7.4$ Hz) and δ_H 5.20 (1H, d, $J = 7.3$ Hz). The ^{1}H and ^{13}C NMR spectral data of **1** showed the presence of two geniposidic acid (**2**) [10] moieties, and thus it was deduced that the carboxyl of unit a was esterified with the hydroxyl at 10b position of unit b (Figure 1). This was proved by the downfielded position of C-10b (δ 63.4) and H-10b (δ 4.93 and 4.79), the upfielded position of C-11a (δ 168.9), and further confirmed by the correlation between H-10b and C-11a in the HMBC spectrum. Since the stereochemistry of the three asymmetric centers (C-1, C-5, and C-9) was the same in practically all iridoids identified hitherto [11], OH-1a, OH-1b, H-5a, H-5b, H-9a, and H-9b were assigned as β-orientation in the iridoid skeleton. The relative configuration of compound **1** was further confirmed by the ROESY correlations in Table 1. Thus, the structure of compound **1** was characterized as shown in Figure 1, and was named scyphiphin D.

Compound **2** was determined as geniposidic acid by comparison of the ^{1}H and ^{13}C NMR spectral data of **2** with those reported in the literature [10].

3. Experimental

3.1 General experimental procedures

Optical rotation was recorded using a Rudolph Autopol III polarimeter (Rudolph Research Analytical, Hackettstown, NJ, USA). The IR spectra were obtained on a Nicolet 380 FT-IR instrument, as KBr pellets. The NMR spectra were recorded on a Bruker AV-400 spectrometer, using TMS as an internal standard. The HR-ESI-MS spectra were measured with an API QSTAR Pulsar mass spectrometer. Column chromatographies (CCs) were performed with silica gel (Marine Chemical Industry Factory, Qingdao, China) and Sephadex LH-20 (Merck, Darmstadt, Germany). TLC was performed with silica gel GF254 (Marine Chemical Industry Factory).

3.2 Plant material

The aerial parts of *S. hydrophyllacea* Gaertn. F. were collected in Wenchang County (Nov. 2004) in Hainan Province (China). It was identified by Associate Prof. Zheng-Fu Dai of the Institute of Tropical Bioscience and Biotechnology, Chinese Academy of Tropical Agricultural Sciences, where a voucher specimen (SH20051112) is deposited.

3.3 Extraction and isolation

The dried, milled aerial parts of *S. hydrophyllacea* Gaertn. F. (17.6 kg) were exhaustively extracted with 95% EtOH (3 × 30 l) at room temperature. After evaporation, the residue was suspended in H_2O and partitioned with light petroleum ether to give a light petroleum ether fraction (687.0 g). The H_2O part was applied to a D101 reticular resin column eluted with H_2O and MeOH. The MeOH eluent was concentrated *in vacuo* to give a residue (421.0 g), which was chromatographed on a silica gel column (200–300 mesh) with $CHCl_3$–MeOH [50:1 (2.6 l), 20:1 (21.5 l), 10:1 (17.5 l), 5:1

Table 1. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectral data and HMBC and ROESY correlations of compound **1** (δ in ppm, J in Hz, CD_3OD).

Position	δ_C	δ_H	HMBC (H → C)	ROESY
1a	98.3 (d)	5.18 (1H, d, 7.4)	C-5a, C-9a, C-1a′, C-8a, C-3a	H-3a, H-1a′, H-6a (α)
3a	153.7 (d)	7.58 (1H, s)	C-5a, C-1a, C-4a, C-11a	H-1a, H-7a
4a	112.6 (s)			
5a	36.6 (d)	3.22 (1H, m)	C-6a, C-9a, C-1a, C-3a, C-11a	H-9a, H-6a (β)
6a	39.8 (t)	2.85 (1H, m, H-β)	C-5a, C-9a, C-7a, C-8a	H-5a, H-9a
		2.13 (1H, m, H-α)	C-5a, C-9a, C-7a, C-8a	H-1a
7a	128.5 (d)	5.80 (1H, br s)	C-5a, C-6a, C-9a, C-10a, C-8a	H-10a
8a	144.7 (s)			
9a	47.1 (d)	2.74 (1H, t, 7.4)	C-5a, C-6a, C-1a, C-7a, C-8a	H-5a, H-10a, H-6a (β)
10a	61.5 (t)	4.31 (1H, d, 14.5)	C-9a, C-7a, C-8a	H-7a, H-9a
		4.19 (1H, dd, 1.2, 14.5)	C-9a, C-7a, C-8a	
11a	168.9 (s)			
1a′	100.6 (d)	4.72 (1H, d, 7.8)	C-1a, C-2a′, C-5a′	H-1a, H-3a′
2a′	74.9 (d)	3.25 (1H, m)	C-1a′, C-3a′	H-4a′
3a′	78.0 (d)	3.39 (1H, m)	C-2a′, C-4a′	H-1a′, H-5a′
4a′	71.6 (d)	3.31 (1H, overlapped)	C-3a′, C-5a′, C-6a′	H-2a′, H-6a′
5a′	78.4 (d)	3.31 (1H, overlapped)	C-1a′, C-6a′, C-4a′	H-1a′, H-3a′
6a′	62.8 (t)	3.86 (1H, d, 11.7)	C-4a′, C-5a′	H-4a′, H-5a′
		3.65 (1H, m)	C-4a′, C-5a′	
1b	98.4 (d)	5.20 (1H, d, 7.3)	C-5b, C-9b, C-1b′, C-8b, C-3b	H-3b, H-1b′, H-6b (α)
3b	153.3 (d)	7.52 (1H, s)	C-5b, C-1b, C-4b, C-11b	H-1b, H-7b
4b	112.6 (s)			
5b	36.4 (d)	3.17 (1H, m)	C-6b, C-9b, C-1b, C-3b, C-11b	H-9b, H-6b (β)
6b	40.0 (t)	2.85 (1H, m, H-β)	C-5b, C-9b, C-7b, C-8b	H-5b, H-9b
		2.13 (1H, m, H-α)	C-5b, C-9b, C-7b, C-8b	H-1b
7b	131.1 (d)	5.84 (1H, br s)	C-5b, C-6b, C-9b, C-10b, C-8b	H-10b
8b	139.8 (s)			
9b	47.7 (d)	2.77 (1H, t, 7.3)	C-5b, C-6b, C-1b, C-7b, C-8b	H-5b, H-10b, H-6b (β)
10b	63.4 (t)	4.93 (1H, d, 14.2)	C-9b, C-7b, C-8b, C-11a	H-7b, H-9b
		4.79 (1H, d, 14.2)	C-9b, C-7b, C-8b, C-11a	
11b	170.9 (s)			
1b′	100.4 (d)	4.72 (1H, d, 7.8)	C-1b, C-2b′, C-5b′	H-1b, H-3b′

Table 1 – *continued*

Position	δ_C	δ_H	HMBC (H → C)	ROESY
2b′	74.8 (d)	3.25 (1H, m)	C-1b′, C-3b′	H-4b′
3b′	77.9 (d)	3.37 (1H, m)	C-2b′, C-4b′	H-1b′, H-5b′
4b′	71.5 (d)	3.31 (1H, overlapped)	C-3b′, C-5b′, C-6b′	H-2b′, H-6b′
5b′	78.4 (d)	3.31 (1H, overlapped)	C-1b′, C-6b′, C-4b′	H-4b′, H-5b′
6b′	62.7 (t)	3.86 (1H, d, 11.7)	C-4b′, C-5b′	H-4b′, H-5b′
		3.65 (1H, m)	C-4b′, C-5b′	

(21.5 l), 2:1 (21.0 l)] to give 26 fractions. Fraction 20 (8.89 g) was subjected to CC over silica gel eluted with $CHCl_3$–MeOH (9:1) to afford eight further fractions. Subfraction 2 (982.1 mg) was fractionated by CC (Sephadex LH-20) eluted with 95% EtOH and then rechromatographed on a silica gel column with $CHCl_3$–MeOH (8:2) to afford compound **2** (429.2 mg). Fraction 21 (17.18 g) was subjected to vacuum liquid CC over RP-18 eluted with MeOH–H_2O [1:9 (0.5 l), 2:8 (0.5 l), 3:7 (0.5 l), 4:6 (0.5 l), 1:1 (0.5 l), 6:4 (0.5 l), 8:2 (0.5 l), 0:1 (0.5 l)] gradually to afford six further fractions. Subfraction 3 (1.41 g) was purified by silica gel CC eluted with $CHCl_3$–MeOH (8:2) to afford compound **1** (885.2 mg).

*3.3.1 Scyphiphin D (**1**)*

White amorphous powder; $[\alpha]_D^{31} + 60.0$ ($c = 1.00$, MeOH); IR (KBr) ν_{max} (cm^{-1}): 3423, 2921, 1691, 1631, 1279, 1200, 1160, 1076, 942, 897; ^1H NMR and ^{13}C NMR spectral data: see Table 1; HR-ESI-MS: m/z 753.2224 $[M + Na]^+$ (calcd for $C_{32}H_{42}O_{19}Na$, 753.2217).

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