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NOTE

A New Cytotoxic Prenylated Chalcone from *Desmodium renifolium*

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A new prenylated chalcone, 2',5-dihydroxy-4,4'-dimethoxy-3-prenyl-chalcone (**1**), was isolated from whole *Desmodium renifolium* plants. Its structure was determined by spectroscopic methods including 1D and 2D NMR. Compound **1** was evaluated for its cytotoxicity using five tumor cell lines ((NB4, A549, SHSY5Y, PC3 and MCF7). It exhibited cytotoxicity against NB4 and MCF7 cell with IC_{50} values of 5.8 and 6.9 μM, respectively.

Keywords: Prenylated chalcone, *Desmodium renifolium*, Cytotoxicity.

Desmodium renifolium (Linn.) Schindl is a dwarf shrub belonging to the *Desmodium* genus of the Leguminosae family[1]. The Dai people of Xishuangbanna prefecture in Yunnan province use it extensively as a diuretic, anti-inflammatory and detoxifying agent[2]. Despite it uses in traditional medicine, no study on the secondary metabolites of *D. renifolium* has been presented in the literature. However, a range of bioactive compounds including flavonoids[3-5], alkaloids[5], terpenoids[5], steroids[5] and phenylpropanoids[5] have been found in other plants from the *Desmodium* genus. Therefore, as part of our ongoing program aimed at identifying bioactive compounds with potential pharmaceutical applications from local plants, we investigated the secondary metabolites produced by *D. renifolium* plants collected in Xishuangbanna prefecture. A new prenylated chalcone (**1**) was isolated in this work.

UV spectra were acquired using a Shimadzu UV-2401A spectrophotometer. A Tenor 27 spectrophotometer was used to acquire IR spectra. 1D- and 2D NMR spectroscopic data were recorded on Bruker DRX-500 spectrometers, using TMS as an internal standard. Chemical shifts (δ) are expressed in ppm relative to the TMS signal. HRESIMS analyses were performed using a VG Autospec-3000 mass spectrometer. Semi-preparative HPLC was performed on a Shimadzu LC-8A preparative liquid chromatograph with Zorbax PrepHT GF (21.2 mm × 25 cm) or Venusil MP C_{18} (20 mm × 25 cm) columns. Column chromatography was performed using silica gel (200-300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, China), Lichroprep RP-18 gel (40-63 μm, Merck, Darmstadt, Germany), Sephadex LH-20 (Sigma-Aldrich, Inc, USA), or MCI gel (75-150 μm, Mitsubishi Chemical Corporation, Tokyo, Japan). Column fractions were monitored by TLC; individual TLC plates were visualized by spraying with 5 % H_2SO_4 in EtOH and heating.

Whole *Desmodium renifolium* (Linn.) Schindl., plants were purchased from the Dai Minority Hospital in Xishuangbanna Prefecture, Yunnan province during September of 2012. The species to which the samples belonged was determined by Prof. Yuan Ning. A voucher specimen (YNNI 12-9-36) was deposited in the herbarium of the Yunnan University of Nationalities.

Extraction and isolation: The combined samples (2.5 kg) were crushed and then filtered through a 30 mesh sieve. The resulting powder was extracted with 70 % aqueous acetone (4 × 10 L) at room temperature and then filtered again. The filtrate was evaporated under reduced pressure and the crude extract (72 g) was passed through a silica gel (150-200 mesh) column, eluting with a $CHCl_3$-MeOH gradient (9:1, 8:2, 7:3, 6:4, 5:5) to afford six fractions (A-E). Further separation of fraction A (42.1 g) by silica gel column chromatography, eluting with petroleum ether-acetone (9:1-1:2), yielded subfractions A1-A6. Subfraction A2 (8:2, 8.45 g) was separated on a silica gel column, eluting with petroleum ether-EtOAc, followed by semi-preparative HPLC (62-65 % MeOH-H_2O, flow rate 12 mL/min) to give compound **1** (8.5 mg).

2',5-Dihydroxy-4,4'-dimethoxy-3-prenyl-chalcone (1): Compound **1** was obtained as a pale yellow gum: UV (MeOH) ν_{max} (log ε) 210 (4.15), 252 (3.52), 362 (3.76) nm; IR (KBr, ν_{max}, cm^{-1}): 3414, 3145, 3072, 2948, 2839, 1685, 1602, 1528, 1469, 1338, 1182, 1065, 894, 783; ^1H and ^{13}C NMR data (500

and 125 MHz, acetone-d_6) in Table-1; positive ESIMS *m/z* 391 $[M + Na]^+$; positive HRESIMS *m/z* 391.1526 $[M + Na]^+$ ($C_{22}H_{24}NaO_5$, Calcd for: 391.1521).

The whole plants of *D. renifolium* were extracted with 70 % acetone. The resulting extracts were then subjected to repeated column chromatography on silica gel, Sephadex LH-20 and RP-18 silica gel. A final purification by semi-preparative RP-HPLC afforded compound **1**. its structure are shown in Fig. 1, while the ^1H and ^{13}C NMR data for compound **1** are presented in Table-1.

TABLE-1
^1H AND ^{13}C NMR DATA OF COMPOUND **1**
(500 AND 125 MHz, ACETONE-d_6)

No.	δ_C	δ_H (m, J, Hz)	No.	δ_C	δ_H (m, J, Hz)
1	126.2 s		1″	25.9 t	3.65, d (6.8)
2	113.5 d	6.72, d 2.2	2″	123.4 d	5.10, t (6.8)
3	143.2 s		3″	132.2 s	1.68, s
4	150.8 s		4″	18.5 q	
5	132.5 s		5″	25.6 q	1.82, s
6	120.4 d	6.95 d (2.2)	α	119.8 d	7.62, d (15.2)
1′	114.8 s		β	143.5 d	8.15, d (15.2)
2′	165.2 s	6.39, d (2.2)	C=O	192.4 s	3.82, s
3′	103.4 d		-OMe-4	61.2 q	
4′	167.5, s	6.45, dd (8.6, 2.2)	-OMe-4′		3.78, s
5′	106.5 d	8.02, d (8.6)	-OH-5	56.3 q	13.12, s
6′	133.8 d		-OH-2′		12.83, s

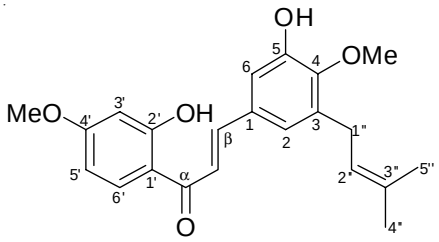

Fig. 1. Structure of compound **1**

Compound **1** was obtained as a pale yellow gum with the molecular formula $C_{22}H_{24}O_5$ as determined by HRESIMS ($[M + Na]^+$ *m/z* 391.1526; Calcd. for 391.1521). Its IR spectrum reveals the presence of a hydroxyl group (3414 cm^{-1}), a conjugated ketone (1685 cm^{-1}) and an aromatic ring (1602, 1528 and 1469 cm^{-1}). Its ^1H NMR spectrum indicates that it contains a 1,2,4-trisubstituted benzene ring [δ_H 6.39 (1H, d, 2.2 Hz), 6.45 (1H, dd, 8.6, 2.2 Hz) and 8.02 (1H, d, 8.6 Hz)], a prenyl group [d_H 3.65 (2H, d, 6.8 Hz), 5.10 (1H, d, 6.8 Hz) and 1.68, 1.82 (each 3H, s)], a 1,3,4,5-tetrasubstituted benzene ring [δ_H 6.72 (1H, d, 2.2 Hz) and 6.95 (1H, d, 2.2 Hz)], a double bond [δ_H 7.62 (1H, d, 15.2), 8.15 (1H, d, 15.2)] and two phenolic hydroxyl groups (δ_H 13.12 and 12.83). The ^{13}C NMR spectrum of compound **1** contains 22 signals, representing two benzene rings, a prenyl group, a disubstituted alkene, two methoxy groups and a carbonyl group. These findings suggest that compound **1** is a prenylated chalcone derivative. Its NMR spectra are very similar to those for 5'-prenyl-butein[6]; the two compounds only differ in that compound **1** has a methoxy group at the C-4' position while 5'-prenylbutein has a hydroxyl group there. In compound **1**, the locations of two methoxy group at C-4 and C-4' were confirmed by HMBC correlations of the 4-OMe group (δ_H 3.82, s) with C-4 (δ_C 150.8) and 4'-OMe group (δ_H 3.78, s) with C-4' (δ_C 167.5) Fig. 2. The HMBC correlations between the hydroxy proton (δ_H 13.12) and C-4 (δ_C 150.8), C-5 (δ_C 132.5) and C-6 (δ_C 120.4), as well as those between the other hydroxy proton (δ_H 12.83) and C-1' (δ_C 114.8), C-2' (δ_C 165.2) and C-3' (δ_C 103.4), led to the assignment of the phenolic hydroxy groups at C-5 and C-2'.

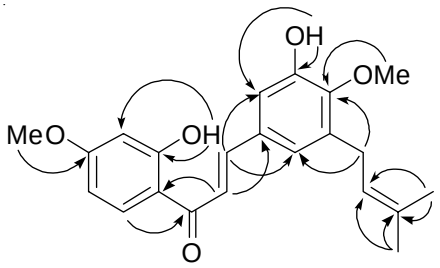

Fig. 2. Selected HMBC correlations compound **1**

Many chalcone derivatives are known to be cytotoxic[7-10]. Compound **1** was tested for its cytotoxicity against five human tumor cell lines (NB4, A549, SHSY5Y, PC3 and MCF7) using the MTT method as reported previously[11]. Taxol was used as the positive control. The results showed that compound **1** exhibited high cytotoxicity against NB4 and MCF7 cell with IC_{50} values of 5.8 and 6.9 μM, respectively.

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