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A new picrotoxane-type sesquiterpene from *Dendrobium findlayanum*

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NOTE

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A new picrotoxane-type sesquiterpene, findlayanin (**1**), was isolated from *Dendrobium findlayanum* with crystallinin (**2**). The structure of compound **1** was established to be (1*R*,2*S*,3*R*,4*S*,5*R*,6*S*,9*R*)-2,3,11,12-tetrahydropicrotoxan-12(15)-lactone by spectroscopic methods.

Keywords: *Dendrobium findlayanum*; findlayanin; crystallinin; picrotoxane-type; sesquiterpene

1. Introduction

Dendrobium is a large and diverse genus of orchids with more than 1500 species distributed throughout the world [1]. In China, many *Dendrobium* sp. are used in traditional or folk medicine as a Yin tonic to nourish the stomach and promote the production of body fluid [2], and studies on the bioactive chemical constituents have led to the isolation of a series of components including alkaloids, bibenzyls, phenanthrenes, sesquiterpenes, and sesquiterpene glycosides. In previous work, 21 sesquiterpenes, belonging to five different types, have been isolated from *D. nobile* [3–6], *D. crystallinum* [7], *D. densiflorum* [8], *D. amoenum* [6], and *D. aduncum* [6]. As one part of our research for bioactive metabolites from natural sources [9–11], the chemical study on *D. findlayanum* was carried out, which led to the isolation of a new picrotoxane-type sesquiterpene, findlayanin (**1**) (Figure 1). In this paper, the

isolation and structural elucidation of findlayanin were described.

2. Results and discussion

Compound **1** was obtained as colorless needles with mp 193–194°C and $[\alpha]_D^{22} - 65.70$ ($c = 0.29$, MeOH). The EI-MS showed a molecular ion peak at m/z 284. The molecular formula was established to be $C_{15}H_{24}O_5$ by HR-EI-MS (m/z 284.1626, $[M]^+$), indicating four degrees of unsaturation. The IR spectrum exhibited strong absorptions at 3345 and 1755 cm^{-1} , which were ascribed to hydroxyl and carbonyl groups, respectively. In ^{13}C NMR and DEPT spectra (Table 1), 15 signals appeared, which were classified into three methyls, three sp^3 methylenes (one of them bearing an oxygen atom), six sp^3 methines (two of them bearing an oxygen atom), two sp^3 quaternary carbons (one of them bearing an oxygen atom), and one ester carbonyl carbon. Interpretation of the

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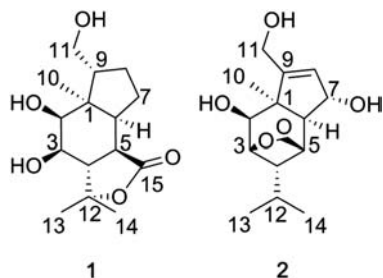


Figure 1. Structures of compounds **1** and **2**.

^1H - ^1H COSY and HSQC spectra revealed a fragment of C-2-C-3-C-4-C-5-C-6-C-7-C-8-C-9-C-11 (Figure 2). The connection between C-4 and C-12 was assigned on the basis of ^1H - ^{13}C long-range correlations from H-13 and H-14 to C-4 and C-12. The HMBC correlations from H-10 to C-2, C-6, and C-9, and from H-6, H-7, H-10, and H-11 to C-1 suggested the connectivities of C-2, C-6, C-1, C-9, and C-10 to C-1. The connection between C-5 and C-15 was established by the HMBC correlations from H-4 and H-5 to C-15. No correlations from H-2 or H-3 or H-11 to C-15 can be observed in HMBC spectrum, implying that the lactone bridge was between C-15 and C-12. The relative configuration was determined on the basis of ROESY data

(Figure 3). ROESY correlations were found between H-10 and H-2, H-6, H-11a, H-11b, and between H-3 and H-2, H-5, H-10, H-13, suggesting that H-2, H-3, H-5, H-6, the methyl group at C-1, the isopropyl group at C-4, and the hydroxyl methyl group at C-9 were all α -oriented, and then the relative stereostructure of compound **1** was assigned as shown in Figure 1. To determine the absolute configuration, CD spectrum was measured, which showed a negative Cotton effect at 217 nm. Application of the octant rule gave the configuration *R* at C-1, C-3, C-5, and C-9, and the configuration *S* at C-2, C-4, and C-6. Thus, compound **1** was elucidated to be (1*R*,2*S*,3*R*,4*S*,5*R*,6*S*,9*R*)-2,3,11,12-tetrahydroxypicrotoxan-12(15)-lactone (Figure 1), which is a new sesquiterpene and named as findlayanin.

3. Experimental

3.1 General experimental procedures

Melting point was measured on an uncorrected X-4 digital melting point apparatus (Gongyi Yuhua Co., Ltd, Gongyi, China). Optical rotation was taken on a Horiba SEPA-300 automatic polarimeter (Horiba, Tokyo, Japan). UV spectrum was recorded

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

Position	δ_{H} (m, <i>J</i>)	δ_{C}
1		50.5
2	3.38 (1H, d, <i>J</i> = 3.2)	79.5
3	3.89 (1H, dd, <i>J</i> = 3.2, 10.7)	71.2
4	2.58 (1H, dd, <i>J</i> = 10.7, 14.8)	46.2
5	2.84 (1H, dd, <i>J</i> = 4.8, 14.8)	42.8
6	2.07 (1H, m)	44.7
7 α	1.66 (1H, m)	26.3
7 β	1.67 (1H, m)	
8 α	1.48 (1H, m)	30.3
8 β	2.06 (1H, m)	
9	2.40 (1H, m)	47.3
10	1.05 (3H, s)	20.1
11a	3.63 (1H, dd, <i>J</i> = 6.4, 10.6)	65.1
11b	3.46 (1H, dd, <i>J</i> = 6.8, 10.6)	
12		87.1
13	1.43 (3H, s)	20.3
14	1.52 (3H, s)	29.6
15		178.6

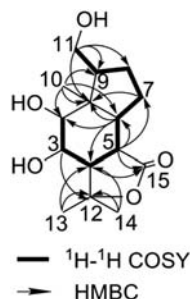


Figure 2. Key ^1H - ^1H COSY and HMBC correlations of compound **1**.

on Shimadzu UV-2401 PC spectrophotometer (Shimadzu, Tokyo, Japan). IR spectrum was obtained on Bruker Tensor 27 spectrometer (Bruker, Karlsruhe, Germany) with KBr pellets. CD spectrum was measured on a Chirascan circular dichroism spectrometer (Applied Photophysics, Leatherhead, UK). NMR spectra were recorded on Bruker AM-400 and DRX-500 spectrometers (Bruker) in CD_3OD , with tetramethylsilane as an internal standard, δ in ppm, J in Hz. EI-MS and HR-EI-MS were recorded using a VG Autospec3000 mass spectrometer (VG, Manchester, England). Silica gel (200–300 mesh, Qingdao Marine Chemical, Inc., Qingdao, China) was used for column chromatography. Pre-coated silica gel

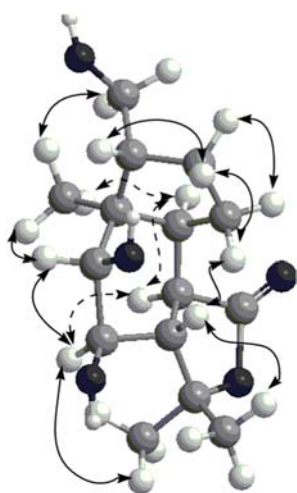


Figure 3. 3D model with NOE correlations of compound **1**.

GF254 plates (Qingdao Marine Chemical, Inc.) were used for TLC. Fractions were monitored by TLC and spots were visualized by heating silica gel plates sprayed with vanillin- H_2SO_4 in ethanol.

3.2 Plant material

The material *D. findlayanum* was collected in Yunnan Tropical Crops Vocational College, Puer, China, in September 2007, and identified by Mrs Ling Ning, Yunnan Tropical Crops Vocational College. A voucher specimen has been deposited in Yunnan Tropical Crops Vocational College.

3.3 Extraction and isolation

The dried whole plants (1.3 kg) of *D. findlayanum* were crushed and extracted with EtOH (10,000 ml \times 3). The combined organic phase was evaporated *in vacuo* to give a deep brown gum (130 g), which was then suspended in water and adjusted to pH 3.0 with 1% hydrochloric acid, and then partitioned with EtOAc (600 ml \times 4), evaporated *in vacuo* to get the corresponding extract (50 g). The EtOAc extract was subjected to silica gel column chromatography (200–300 mesh, 6.0 \times 60 cm) and eluted with CHCl_3 -MeOH gradient (from 100:0 to 0:100, v/v) to afford fractions A–M. Fraction C (6.3 g), eluted with CHCl_3 -MeOH (98:2, v/v), yielded colorless needles which were further purified by re-crystallization in MeOH to give crystallin (**2**, 110.8 mg). Fraction J (2.1 g), eluted with CHCl_3 -MeOH (8:2, v/v), was subjected to silica gel column chromatography, eluted with gradients of CHCl_3 and MeOH (from 100:0 to 0:100, v/v), and then findlayanin (**1**, 17.5 mg) was obtained from the fraction of CHCl_3 -MeOH (9:1, v/v) and further purified by re-crystallization in MeOH.

3.3.1 Findlayanin (**1**)

Colorless needles; mp 193–194°C; $[\alpha]_{\text{D}}^{22} - 65.7$ ($c = 0.29$, MeOH); IR (KBr) ν_{max} : 3345 (OH), 1755 (lactone, C=O) cm^{-1} ;

CD (MeOH) $\Delta\epsilon_{217\text{ nm}} - 1.622$; ^1H and ^{13}C NMR spectral data, see Table 1. EI-MS m/z (%): 284 [M^+] (7), 213 (20), 182 (88), 85 (100), 69 (60); HR-EI-MS m/z : 284.1626 [M^+] (calcd for $\text{C}_{15}\text{H}_{24}\text{O}_5$, 284.1624).

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