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## NOTE

### A new picrotoxane-type sesquiterpene from *Dendrobium findlayanum*

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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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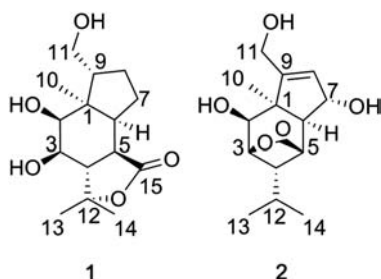


Figure 1. Structures of compounds **1** and **2**.

$^1\text{H}$ – $^1\text{H}$ 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  $^1\text{H}$ – $^{13}\text{C}$  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  $\alpha$ -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-tetrahydroypicrotoxan-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.  $^1\text{H}$  (400 MHz) and  $^{13}\text{C}$  NMR (100 MHz) spectral data of **1** (MeOD,  $\delta$  in ppm, *J* in Hz).

Position	$\delta_{\text{H}}$ (m, <i>J</i> )	$\delta_{\text{C}}$
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 $\alpha$	1.66 (1H, m)	26.3
7 $\beta$	1.67 (1H, m)	
8 $\alpha$	1.48 (1H, m)	30.3
8 $\beta$	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

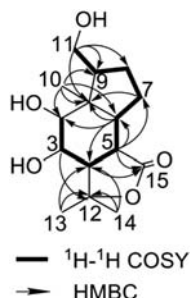


Figure 2. Key  $^1\text{H}$ - $^1\text{H}$  COSY and HMBC correlations of compound **1**.

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  $\text{CD}_3\text{OD}$ , with tetramethylsilane as an internal standard,  $\delta$  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

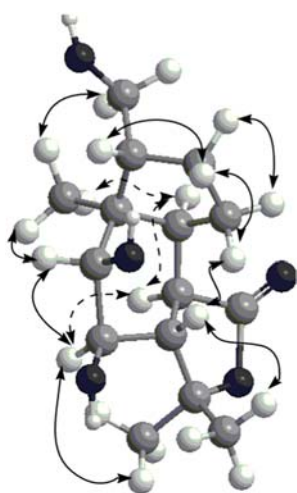


Figure 3. 3D model with NOE correlations of compound **1**.

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- $\text{H}_2\text{SO}_4$  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  $\text{CHCl}_3$ -MeOH gradient (from 100:0 to 0:100, v/v) to afford fractions A–M. Fraction C (6.3 g), eluted with  $\text{CHCl}_3$ -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  $\text{CHCl}_3$ -MeOH (8:2, v/v), was subjected to silica gel column chromatography, eluted with gradients of  $\text{CHCl}_3$  and MeOH (from 100:0 to 0:100, v/v), and then findlayanin (**1**, 17.5 mg) was obtained from the fraction of  $\text{CHCl}_3$ -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)  $\nu_{\text{max}}$ : 3345 (OH), 1755 (lactone, C=O)  $\text{cm}^{-1}$ ;

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

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