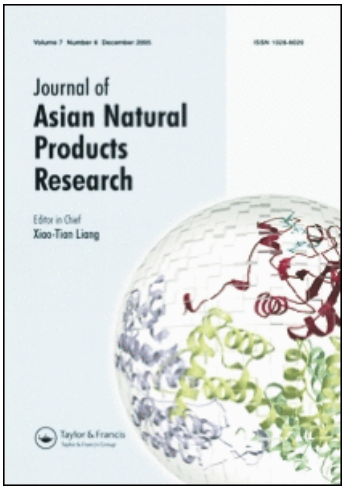

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Note

A NEW SESQUITERPENE GLYCOSIDE FROM *DENDROBIUM NOBILE* LINDL.

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A new sesquiterpene glycoside with a picrotoxane-type aglycone has been isolated from the stems of *Dendrobium nobile* Lindl. Its structure was elucidated as 7,12-dihydroxy-5-hydroxymethyl-11-isopropyl-6-methyl-9-oxatricyclo[6.2.1.$0^{2,6}$]undecan-10-one-15-*O*-β-D-glucopyranoside on the basis of spectroscopic data and chemical methods.

Keywords: *Dendrobium nobile*; Sesquiterpene glycoside

INTRODUCTION

In traditional Chinese medicine, the stems of *Dendrobium* sp. are used to nourish the stomach, promote secretion of saliva, and reduce fever [1]. *Dendrobium nobile* Lindl. is one of the most famous *Dendrobium* plants used as a tonic. In previous reports, alkaloids, phenanthrenes, fluorenones, bibenzyls and sesquiterpene glycosides have been isolated from this plant [2–10]. Among them, some constituents exhibited antitumor, antimutagenic, and immunomodulatory activities [6,7,9,10]. Here we report the isolation and structure determination of a new sesquiterpene glycoside obtained from the n-BuOH fraction of the plant.

RESULTS AND DISCUSSION

Compound **1** was obtained as a white amorphous powder. Its molecular formula was established as $C_{21}H_{34}O_{10}$ by HR-ESIMS and NMR spectra; it has five degrees of unsaturation. The IR spectrum displayed hydroxyl and lactonic carbonyl absorption bands at 3423 and 1759 cm^{-1} respectively. In the ^{1}H and ^{13}C NMR spectra, one anomeric proton and anomeric

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carbon signals appeared at δ 4.86 (d, $J = 7.5$ Hz) and δ 104.5, respectively. On acidic hydrolysis, it afforded D-glucose. The stereochemistry for the glucose was assigned a β configuration on the basis of the coupling constant ($J = 7.5$ Hz) of the anomeric proton. The ^{13}C NMR showed fifteen carbons of the aglycone: three methyls (δ 22.6, 29.9, 30.3), three methylenes (δ 26.4, 28.9, 73.4), six methines (δ 43.7, 44.9, 46.4, 53.8, 73.0, 85.1) and three quaternary carbons (δ 50.0, 68.6, 179.4). As two unsaturated functionalities were D-glucose and a carbonyl group (δ 179.4), the aglycone had to be tricyclic. Analysis of the HMQC data for compound **1** showed that the protons at δ 4.94 (1H, brs), 5.05 (1H, brd, $J = 4.5$ Hz), 2.36 (1H, t, $J = 4.5$ Hz), 2.69 (1H, t, $J = 4.0$ Hz), 3.20 (1H, m), 2.03 (2H, m) and 3.54 (1H, m) corresponded to the carbons at the δ 73.0, 85.1, 53.8, 46.4, 44.9, 26.4 and 43.7 respectively; the protons at δ 1.61 (1H, m) and 2.40 (1H, m) to the carbon at δ 28.9; and the protons at δ 4.20 (1H, dd, $J = 9.5$, 9.5 Hz) and 4.50 (1H, dd, $J = 9.5$, 5.5 Hz) to the carbon at δ 73.4. The fragment $(CH)_5$—$(CH_2)_2$—CH<CH_2 was further deduced in its aglycone by the correlations of the proton at δ5.05 with the protons at δ 4.94, 2.36; the proton at δ 2.69 with the protons at δ 2.36, 3.20; the proton at δ 2.03 with the protons at δ 3.20, 1.61, 2.40; and the proton at δ 3.54 with the protons at δ 1.61, 2.40, 4.20, 4.50. From the HMBC spectrum, the protons of a singlet methyl (δ 1.34) had long-range correlation with three methine carbons (δ 43.7, 44.9, 73.0), which indicated the fragment CH_3—C—$(CH)_3$; the protons of the other two single methyls (δ 1.35, 1.37) had correlations with a methine carbon (δ 53.8) and a quaternary carbon (δ 68.6), suggesting the presence of a $(CH_3)_2$—C<CH fragment. The long-range correlations between the carbonyl (δ 179.4) and two methine protons (δ 2.69, 5.05) revealed a lactonic group, which were further supported by the absorption band at 1759 cm^{-1} in the IR spectrum. The substituted position of the D-glucose was assigned by the correlation of C-15/H-1′ in the HMBC spectrum. The ^{1}H NMR data of compound **1** and the data of dendroside G, which has an aglycone with a picrotoxane-type sesquiterpene skeleton, are similar except for δ1.13 (Me-14, d, $J = 6.2$ Hz), 1.15 (Me-13, d, $J = 6.2$ Hz), 2.05 (H-12, t, $J = 6.6$, 6.6 Hz), 2.75 (H-1, d, $J = 3.5$ Hz), 5.02 (H-8, s) [10]. Combined with the HMBC spectra, the structure of compound **1** was deduced to be similar to dendroside G. The difference lies in the substitution of a hydroxyl group at C-12 in the aglycone but not at C-11.The relative configuration of the aglycone was characterized on the basis of NOE correlations between H-2 and H-1, H-3, H-7, Me-13, Me-14, Me-16; H-7 and H-8, Me-16; and H-15a and H-1′, H-4a, H-5, Me-16. Compound **1** was finally established as 7,12-dihydroxy-5-hydroxymethyl-11-isopropyl-6-methyl-9-oxatricyclo[6.2.1.0^{2,6}]undecan-10-one-15-*O*-β-D-glucopyranoside (Fig. 1).

EXPERIMENTAL

General Experimental Procedures

The IR spectrum was recorded on a Perkin-Elmer 683 FT infrared spectrometer. Optical rotation was measured on a Perkin-Elmer 241 polarimeter. NMR spectra were run on a Varian INOVA-500 NMR spectrometer with TMS as internal standard. FABMS was measured on a ZABSPECE mass spectrometer. The HR-ESIMS was obtained on a Bruker Apex II. FT-ICR mass spectrometer.

Plant Material

Fresh stems of *Dendrobium nobile* were obtained from the Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and identified by Professor Shun-Xing Guo. A voucher specimen (No. 20011023) has been deposited in the Department of Fungus, Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences.

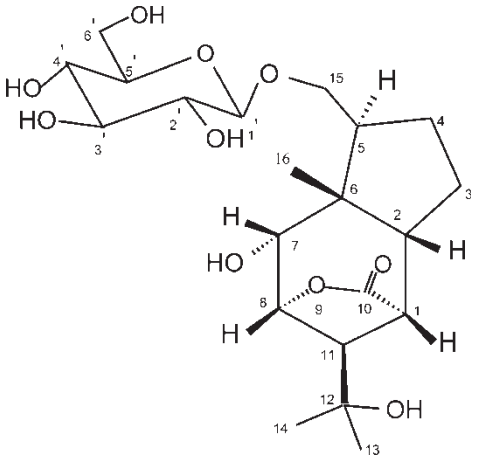

FIGURE 1 Structure of compound **1**.

Extraction and Isolation

The powdered air-dried stems of *Dendrobium nobile* (2.5 kg) were refluxed three times with 95% EtOH. After removing the EtOH under reduced pressure, the residue was partitioned between water and light petroleum, CH_2Cl_2, EtOAc and n-BuOH successively. The n-BuOH extract (75 g) was separated on a silica gel column (mesh 100–200), eluting with $CHCl_3$–MeOH–water (7:3:1) to afford eight fractions. Fraction 5 was further subjected to a silica gel column (mesh 100–200) for chromatography and eluted with $CHCl_3$–MeOH (85:15) to give a further nineteen fractions, of which fraction 13 was loaded on Lobar RP-18 columns eluted

TABLE I NMR data for the compound **1** in C_5D_5N

Position	*^{1}H (multi., J in Hz)*	*^{13}C*	*COSY*	*HMBC*	*NOE*
1	2.69 (t, 4.0)	46.4 d	H-2,11	C-2,3,6,8	
2	3.20 (m)	44.9 d	H-1,3	C-1,4,5,6,16	H-1,3,7; Me-13,14,16
3	2.03 (m)	26.4 t	H-2,4	C-1,2,4,5,6	
4a	1.61 (m)	28.9 t	H-3,4b,5	C-3,5,15	
4b	2.40 (m)		H-3,4a,5	C-3,5,6,15	
5	3.54 (m)	43.7 d	H-4,15	C-4,6,15,16	
6		50.0 s			
7	4.94 (brs)	73.0 d	H-8	C-5,6,8,15	H-2,8; Me-15
8	5.05 (brd, 4.5)	85.1 d	H-7,11	C-1,6,7,11	
10		179.4 s			
11	2.36 (t, 4.5)	53.8 d	H-1,8	C-2,8,12	
12		68.6 s			
13	1.35 (s)	29.9 q	H-14	C-11,12,14	
14	1.37 (s)	30.3 q	H-13	C-11,12,13	
15a	4.20 (dd, 9.5, 9.5)	73.4 t	H-5,15b	C-4,5,6	H-1′,4a,5;Me-16
15b	4.50 (dd, 9.5, 5.5)		H-5,15a	C-4,5,6	
16	1.34 (s)	22.6 q		C-2,5,6,7	
1′	4.86 (d, 7.5)	104.5 d	H-2′	C-3′,5′,15	
2′	3.99 (t, 8)	74.8 d	H-1′, 3′	C-3′	
3′	4.19 (t, 8.5)	78.2 d	H-2′,4′	C-2′,4′	
4′	4.22 (t, 8.5)	71.2 d	H-3′,5′	C-3′,5′,6′	
5′	3.88 (m)	78.2 d	H-4′,6′	C-3′,4′	
6′a	4.37 (brd, 11.0)	62.4 t	H-5′,6′b	C-4′,5′	
6′b	4.52 (brd, 11.0)		H-5′,6′a	C-4′,5′	

with a MeOH–H_2O step gradient (1:3 to 1:1) to give twenty-three fractions—fraction 4 was separated on an RP-18 column eluted with 10% CH_3CN to give compound **1** (25.2 mg).

Compound **1**, a white amorphous powder; $[\alpha]_{20}^{D}$ −27.9 (*c* 1.63, CH_3OH); IR (KBr) ν_{max} (cm^{-1}): 3423 (OH), 2968, 2879, 1759 (C═O), 1631, 1471, 1361, 1161, 1078, 962, 916, 827, 646; ^1H NMR (500 MHz, C_5D_5N) data and ^{13}C NMR (125 MHz, C_5D_5N) data see Table I; FABMS *m/z*: 469 $[M + Na]^+$; HR-ESIMS *m/z*: 469.2047 ($[M + Na]^+$, calcd. for $C_{21}H_{34}O_{10}Na$, 469.2044).

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