Moniline, a new alkaloid from *Dendrobium moniliforme*

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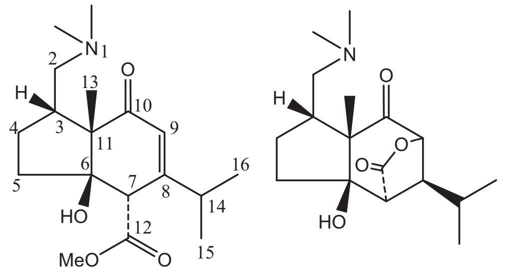
A new alkaloid, moniline (**1**), and a known alkaloid 6-hydroxynobiline (**2**) were isolated from the stems and leaves of *Dendrobium moniliforme*. The structure of **1** was established by spectroscopic methods, especially 2D NMR techniques.

Keywords: *Dendrobium moniliforme*, alkaloids, Chinese medicine

The genus *Dendrobium* is represented by more than 1100 species that are widely distributed throughout Asia, Europe and Australia, thus being the richest genus of the family Orchidaceae. There are 74 species and two variations of *Dendrobium* plants found in China and about 30 species are used in traditional or folk medicine in China as a Yin tonic to nourish the stomach, promote the production of body fluids and reduce fever.[1] The stems of *Dendrobium moniliforme* (L.) Sw. (Orchidaceae) are used in traditional Chinese medicine to reduce fever and as a sialogogue.[2] Previous studies on the biological and chemical constituents of *Dendrobium moniliforme* resulted in the isolation of sesquiterpenes,[3] stilbenoid,[4-5] phenanthraquinones,[6] some of which have exhibited immunoregulatory,[3–4] and anti-inflammatory activities.[6] In the current search for biologically active compounds from Chinese medicinal plants, a new alkaloid named as moniline (**1**) and one known alkaloid 6-hydroxynobiline (**2**) were isolated from this plant. We report the isolation and structural determination of these compounds from *D. moniliforme*.

Compound **1** was obtained as a colourless oil. Its molecular formula, $C_{18}H_{29}NO_4$ [HR-ESIMS *m/z* 324.2180 (Calcd. for $C_{18}H_{30}NO_4$ $[M + 1]^+$ 324.2175), indicated the existence of five degrees of unsaturation in **1**. In the IR spectrum, absorption bands at 3370, 1733, and 1635 cm^{-1} indicated the presence of a hydroxyl, carbonyl, and double bond, respectively. The ^1H NMR spectrum (Table 1) of **1** showed the presence of a double bond proton at δ 5.54 (1H, s), three methyls at δ 0.97 (3H, d, $J = 7.1$ Hz), 1.08 (3H, d, $J = 7.1$ Hz) and 1.16 (3H, s). One methoxy at δ 3.69 (3H, s) and two methyls linked with nitrogen (δ 2.76 6H, s) were also observed in the ^1H NMR spectrum (Table 1) of **1**. Eighteen carbon signals corresponding to the 18 carbon atoms in the molecular formula were all resolved in the ^{13}C NMR spectrum. They comprised five quaternary carbons (two carbonyls at δ 200.0, 174.4), four tertiary carbons, three secondary carbons and six methyls (one oxygenated and two nitrogenated). Two carbonyl groups and one double bond accounted for three degrees of unsaturation, the remaining two degrees of unsaturation were assumed for the presence of a bicyclic system in **1**.

Analysis of the ^1H NMR, ^{13}C NMR and HMQC spectra of **1** enabled us to assign the attachment of all the protons to their respective carbons. The two partial structures **a** (C-2 to C-5), **b** (C-14 to C-16) drawn with bold bond were established by $^1H–^1H$ COSY spectra (Fig. 2). The planar structure of **1** was deduced from HMBC spectra. In the HMBC spectrum (Fig. 2), the HMBC correlations of H-9/C-10 and H-9/C-8 revealed the presence of α, β–unsaturated ketone, which was confirmed by the UV absorption band at 235 nm (logε 3.47). The proton signal of H-7 (δ 3.75) was correlated with the carbon signal at δ 80.8 (C-6), 43.5 (C-5) revealed the linkage of C-5 and C-7 by C-6. The linkage of C-3 and C-10 by the quaternary carbon C-11 was tentatively established by the HMBC correlations of H_3-13/C-3, H_3-13/C-10 and H_3-13/C-11. In the same way, the linkage of C-8 and C-14 was deduced by the HMBC spectrum. The planar structure of **1** was thus established.



1 **2**

Fig. 1 Structure of compounds **1** and **2**.

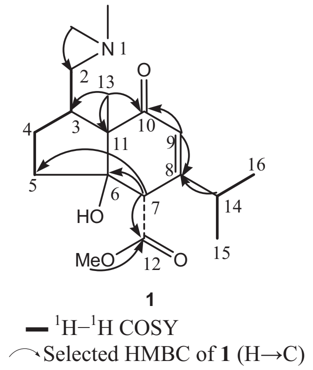


Fig. 2 Selected 2D NMR correlations of **1**.

The relative stereochemistry of **1** was deduced from the NOESY correlation. In the NOESY spectrum, the correlations of H-13/H-7 and H–13/H-3 indicated that the protons of H-3, H-7 and H_3-13 were in the same side of the molecule and defined as β-orientation. As a consequence, the ester group (COOMe) had the α-configuration. The ^1H, ^{13}C NMR spectral data and 2D NMR experiments support the assignment of structure **1** to the new compound which was named moniline.

Compound **2** was identified as 6-hydroxynobiline by comparison the NMR data with literature data.[7] There was no ^{13}C NMR data reported in the literature, so here we also give the ^{13}C NMR data of 6-hydroxynobiline (Table 1).

Experimental

Optical rotations were determined on a Perkin-Elmer 341 polarimeter. IR spectra were recorded on a Perkin-Elmer 577 spectrometer with KBr disks. NMR spectra were measured on a Bruker AM-400 spectrometer with TMS as internal standard. ESIMS was recorded on a Finnigan LCQ^{DECA} Mass spectrometer. All solvents used were of analytical grade (Shanghai Chemical Plant, Shanghai, P.R. China).

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Table 1 NMR data of **1** and **2** at 400 MHz

NO	**1**^{a} (δ_H)	**1**^{a} (δ_C)	**2**^{b} (δ_C)
2	3.02 (1H, m)	61.9	61.2
3	2.50 (1H, m)	34.1	35.4
4	2.12 (2H, m)	29.0	28.1
5	2.05 (1H, m) 2.80 (1H, m)	42.5	41.5
6	–	80.8	83.9
7	3.75 (1H, s)	48.2	54.5
8	–	156.3	51.8
9	5.54 (1H, s)	132.5	83.2
10	–	200.0	207.4
11	–	59.1	59.2
12	–	174.4	175.6
13	1.16 (3H, s)	18.6	19.3
14	2.02 (1H, m)	27.7	25.4
15	0.97 (1H, d, 7.1)	19.7	22.0
16	1.08 (3H, d, 7.1)	20.1	23.7
N–Me	2.76 (6H, s)	44.8	45.5
OMe	3.69 (3H, s)	53.0	–

^{a}Measured in CD_3OD; ^{b}measured in $CDCl_3$.

Silica gel (200–300 mesh) was used for column chromatography, and a precoated silica gel GF_{254} plate (Qingdao Haiyang Chemical Plant, Qingdao, P.R. China) was used for TLC. Amino silica gel (NH-DM 1020, 20–45 μm, Fuji Silysia Chemical Ltd.) was used for column chromatography.

Plant material

Dendrobium moniliforme (L.) Sw. was collected from Lijiang area in Yunnan Province of P. R. China and identified by Yun-Fen Hua of the Zhejiang University of Technology. A voucher specimen (ZJUT 06531) was deposited at Zhejiang University of Technology, P.R. China.

Extraction and isolation

The dry whole plant (650 g) of *D. moniliforme* was ground and percolated with 95% ethanol. After removal of the ethanol under reduced pressure, the crude extract was dissolved in 1 l water to form a suspension and then acidified with 0.5 N H_2SO_4 to pH≈5. The acidic suspension was immediately extracted with ethyl acetate (6 × 300 ml) to remove the non-alkaloid components. The acidic aqueous phase was adjusted with 1N Na_2CO_3 to pH≈10 and extracted with chloroform (6 × 300 ml) to give the crude alkaloids (320 mg). The crude alkaloid fraction was then subjected to a silica gel column (2.5 × 45 cm) eluted with $CHCl_3$/MeOH (20:1–10:1) to collect two major fractions 1 and 2. Fraction 1 (130 mg) was separated by column chromatography packed with amino silica gel and eluted with $CHCl_3$/MeOH (20:1) to yield alkaloid **1** (15 mg). Fraction 2 (80 mg) was also separated by column chromatography packed with amino silica gel and eluted with cyclohexane–EtOAc (4:1) to afford alkaloid **2** (26 mg).

Moniline (**1**), colourless oil, $[\alpha]^{20}_D$ + 68.2° (*c* 0.41, CH_3OH); UVmax (CH_3OH): 235 (3.47); IR (KBr): 3370, 2968, 1733, 1635, 1463, 1389, 1063, 953 cm^{-1}; ESIMS *m/z*: 324 $[M + 1]^+$; HR-ESIMS *m/z*: 324.2180 $[M + 1]^+$ (Calcd. for $C_{18}H_{30}NO_4$ 324.2175). ^1H NMR and ^{13}C NMR data: see Table 1.

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