SHORT REPORT

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Two New Bibenzyl Compounds from *Dendrobium lindleyi*

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Abstract: Two new bibenzyl compounds 4,4',5-trihydroxy-3,3',α-trimethoxybibenzyl (**1**) and 4,5-dihydroxy-3, 3',4',α-tetramethoxybibenzyl (**2**), along with seven known compounds (**3**–**9**), were isolated from the methanol extract of the whole parts of *Dendrobium lindleyi*. The chemical structures were established on the basis of spectroscopic analysis including one and two-dimensional NMR spectroscopy and comparison with previously reported data.

Keywords: Orchidaceae; *Dendrobium lindleyi* ; bibenzyl compound.

1. Plant source

Dendrobium lindleyi (Orchidaceae), mainly distributed among southwest region of China, is not only an ornamental but also a medicinal plant [1]. The plant was collected from Lincang City, Yunnan province, People's Republic of China, in July 2017, and identified as *D. lindleyi* by Prof. Fa-Ming Wu, Zunyi Medical University. A voucher specimen (ZMCNO. 20170716) was deposited with the herbarium of the School of Pharmacy, Zunyi Medical University.

2. Previous Studies

No systematic chemical constitution investigation studies have been reported so far for *Dendrobium lindleyi*. Previous phytochemical investigations on *Dendrobium* showed that phenanthrenes, bibenzyls, alkaloids, fluorenones, sesquiterpenoids, and caffeoylglucose compounds were the main composition [2-7].

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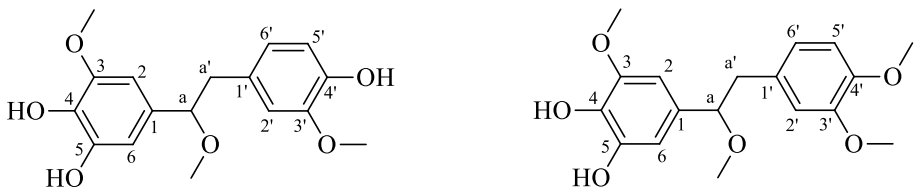
3. Present Study

Dried and powdered whole parts of *D. lindleyi* (705 g) was extracted with 90% methanol under reflux three times (each 3 h) to give an extract (66 g), which was suspended in H_2O (2 L) and extracted with petroleum ether (3×2 L), EtOAc (3×2 L) and n-BuOH (3×2 L) successively. After removing the solvent to obtain the petroleum ether extract (6 g), the ethyl acetate extract (8 g) and the n-butanol extract (13 g), respectively. The petroleum ether extract and ethyl acetate extract were combined and separated by silica gel medium pressure CC (49×460 mm, petroleum ether-acetone 10:1→1:1) to give twenty fractions (Fr.1–20). Fr.13 was purified by semi-preparative HPLC eluted with 70% methanol (5.0 mL/min) to afford four subfractions (Fr.13.1–13.4), Fr.13.1 was further separated by semi-preparative HPLC eluted with 60% methanol (4.0 mL/min) to obtain 4,4'-dihydroxy-3,3',5-trimethoxybibenzyl (21.3 mg) [8] and 3',4-dihydroxy-3,4',5-trimethoxybibenzyl (22.1 mg) [9]. Fr.13.2 was further separated by semi-preparative HPLC eluted with 45% methanol (6.0 mL/min) to obtain 4',5-dihydroxy-3,3'-dimethoxybibenzyl (7.8 mg) [10]. Fr.13.3 was further separated by semi-preparative HPLC eluted with 60% methanol (6.0 mL/min) to give 7-hydroxy-2,8-dimethoxy-1,4-diphenanthraquinone (2.0 mg) [11]. Fr.17 was purified by semi-preparative HPLC eluted with 80% methanol (3.0 mL/min) to afford four subfractions (Fr.17.1–17.4), Fr.17.2 was further separated by semi-preparative HPLC eluted with 60% methanol (6.0 mL/min) to give compounds **1** (8.1 mg) and **2** (2.0 mg). Fr.17.4 was further separated by semi-preparative HPLC eluted with 65% methanol (5.0 mL/min), to obtain 7-hydroxy-2-methoxy-1,4-diphenanthraquinone (1.6 mg) [12]. Fr.6 was purified by semi-preparative HPLC eluted with 98% methanol (4.0 mL/min) to give 2,4-di-tert-butyl phenol ether (13.2mg) [13]. Fr.5 was purified by recrystallization to give *β*-sitosterol (15.0 mg) [14].

4,4',5-trihydroxy-3,3',α-trimethoxybibenzyl ***(1)****:* Brown gum; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.75 (1H, dd, *J* = 13.4 Hz, 5.7 Hz, H-*α*'), 2.97 (1H, dd, *J* = 13.4 Hz, 7.3 Hz, H-*α*'), 3.17 (3H, s, *α*-OMe), 3.77 (3H, s, 3'-OMe), 3.80 (3H, s, 3-OMe), 4.12 (1H, m, H-*α*), 6.30 (1H, br.s, H-2), 6.47 (1H, br.s, H-6), 6.53 (1H, br.s, H-2'), 6.59 (1H, br.d, *J* = 8.0 Hz, H-6'), 6.76 (1H, d, *J* = 8.0 Hz, H-5'); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 44.6 (CH_2, C-*α*'), 56.1 (CH_3, 3'-OMe), 56.4 (CH_3, 3-OMe), 56.9 (CH_3, *α*-OMe), 85.5 (CH, C-*α*), 101.7 (CH, C-2), 107.6 (CH, C-6), 112.5 (CH, C-2'), 114.1 (CH, C-5'), 122.3 (CH, C-6'), 130.6 (C, C-1'), 131.9 (C, C-4), 133.8 (C, C-1), 143.9 (C, C-4'), 144.1 (C, C-5), 146.2 (C, C-3'), 147.1 (C, C-3); HR-ESI-MS: *m/z* 319.1164 $[M–H]^-$ (calcd. for $C_{17}H_{19}O_6^-$, 319.1182).

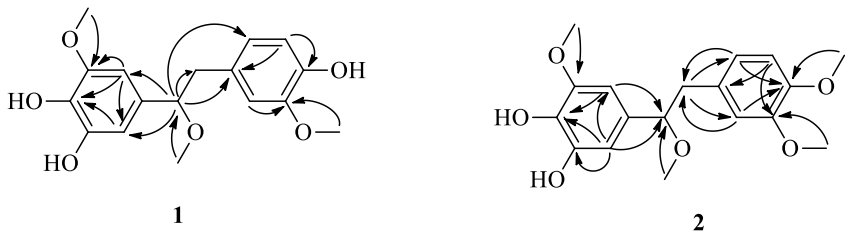
4,5-dihydroxy-3,α,3',4'-tetramethoxybibenzyl ***(2)****:* Brown gum; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.78 (1H, dd, *J* = 13.7 Hz, 5.8 Hz, H-*α*'), 2.99 (1H, dd, *J* = 13.7 Hz, 7.3 Hz, H-*α*'), 3.18 (3H, s, *α*-OMe), 3.77 (3H, s, 3'-OMe), 3.80 (3H, s, 3-OMe), 3.82 (3H, s, 4'-OMe), 4.13 (1H, br.t, *J* = 6.5 Hz, H-*α*), 6.31 (1H, br.s, H-2), 6.48 (1H, br.s, H-6), 6.57 (1H, br.s, H-2'), 6.63 (1H, br.d, *J* = 8.1 Hz, H-6'), 6.73 (1H, d, *J* = 8.1 Hz, H-5'); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 44.5 (CH_2, C-*α*'), 55.9 (CH_3, 3'-OMe), 56.0 (CH_3, 4'-OMe), 56.4 (CH_3, 3-OMe), 56.9 (CH_3, *α*-OMe), 85.4 (CH, C-*α*), 101.6 (CH, C-2), 107.6 (CH, C-6), 111.0 (CH, C-5'), 113.0 (CH, C-2'), 121.6 (CH, C-6'), 131.3 (C, C-1'), 131.8 (C, C-4), 133.8 (C, C-1), 143.8 (C, C-5), 147.1 (C, C-3), 147.5 (C, C-4'), 148.6 (C, C-3'); HR-ESI-MS: *m/z* 333.1336 $[M–H]^-$ (calcd. for $C_{18}H_{21}O_6^-$, 333.1338).



1 **2**

Figure 1. The structures of compounds **1** and **2**

Compound **1** was obtained as a brown gum. Its molecular formula was determined to be $C_{17}H_{20}O_6$ on the basis of HR-ESI-MS at *m/z* 319.1164 $[M-H]^-$, (calcd for $C_{17}H_{19}O_6^-$, 319.1182), indicating 8 degrees of unsaturation. The IR (KBr) spectrum showed absorption band due to hydroxyl group (3420 cm^{-1}). The ^1H NMR spectrum showed the presence of an aromatic ring AMX system signals at δ_H 6.59 (1H, br d, J = 8.0), 6.76 (1H, d, J = 8.0 Hz), and 6.53 (1H, br s), two *meta*-coupled proton signals at δ_H 6.30 (1H, br. s) and 6.47 (1H, br. s), three methoxyl singlet peaks at δ_H 3.80, 3.77, and 3.17 (each 3H, s), an oxygenated multiplet peak at δ_H 4.12 (1H, m), as well as two mutual coupled proton signals at δ_H 2.75 (1H, dd, J = 13.4, 5.7 Hz) and 2.97 (1H, dd, J = 13.4, 7.3 Hz). The ^{13}C NMR and HSQC spectra exhibited 17 carbon signals, including twelve aromatic down-field signals at δ_C 101.7–147.1, an oxygenated tertiary carbon signal at δ_C 85.5, three methoxyl signals at δ_C 56.1, 56.4, 56.9, and a secondary carbon signal at δ_C 44.6. These NMR data above showed that compound **1** has a bibenzyl skeleton [10]. The HMBC correlations (Figure 2) of H-α (δ_H 4.12) with C-α', with C-2, with C-6, with C-1', with C-6', and H-2 (δ_H 6.30) with C-4, with C-6, H-6 (δ_H 6.47) with C-4, H-5' (δ_H 6.76) with C-1' and with C-4', OCH_3 (δ_H 3.17) with C-α (δ_C 85.5) indicated that one methoxyl was located at C-α. The HMBC correlations of OCH_3 (δ_H 3.80) to C-3 (δ_C 147.1), H-2 to C-3, OCH_3 (δ_H 3.77) to C-3' (δ_C 146.2), H-2' to C-3', H-5' to C-3', positioned the another two OCH_3 at C-3 and C-3', respectively. Compound **1** was presumed to be a mixture of enantiomers, because its optical rotation value was approximate to zero [15]. The structure of compound **1** was identified already from *D. loddigesii* Rolfe. in a patent, but the spectral data were no reported in detail. Accordingly, the structure of compound **1** was established as 4,4',5-trihydroxy-3,3',α-trimethoxybibenzyl.



1 **2**

Figure 2. Key HMBC correlations of compounds **1** and **2**

Compound **2** was obtained as a brown gum. Its molecular formula was determined to be $C_{18}H_{22}O_6$ on the basis of HR-ESI-MS at *m/z* 333.1336 $[M-H]^-$, (calcd for $C_{18}H_{21}O_6^-$, 333.1338), indicating 8 degrees of unsaturation. The IR (KBr) spectrum showed absorption band due to hydroxyl group (3420 cm^{-1}). The ^1H NMR spectrum showed the presence of an aromatic ring ABX system, two *meta*-coupled proton signals, four methoxyl signals, an oxygenated methylene signal, as well as two mutual coupled proton signals. The ^{13}C NMR and HSQC spectra exhibited 18 carbon signals, including twelve aromatic down-field signals at δ_C 101.6–148.6, an oxygenated tertiary carbon signal at δ_C 85.4, four methoxyl signals at δ_C 55.9, 56, 56.4, 56.9, and a secondary carbon signal at δ_C 44.5. These NMR data above were very similar to compound **1** except for the addition of a methoxyl signal. The HMBC correlations (Figure 2) of H-α (δ_H 4.13) to C-α', to C-2, to C-6 and H-5' (δ_H 6.73) to C-1', to C-3', OCH_3 (δ_H 3.18) to C-α (δ_C 85.4) indicated that one methoxyl was located at C-α. The HMBC correlations of OCH_3 (δ_H 3.80) to C-3 (δ_C 147.1), H-2 to C-3, OCH_3 (δ_H 3.77) to C-3' (δ_C 148.6), H-2' to C-4', to C-6', to C-α', H-5' to C-1', to C-3', positioned another three OCH_3 at C-3, C-3', and C-4', respectively. Compound **2** was also presumed to be a mixture of enantiomers, as its optical rotation value was approximate to zero. Accordingly, the structure of compound **2** was established as 4,5-dihydroxy-3,α,3',4'-tetramethoxybibenzyl.

Compounds **1** and **2** were new secondary metabolites of *Dendrobium*, and bibenzyl compounds were distributed widely in the stems and leaves of *Dendrobium* [16]. 4,4'-Dihydroxy-3,3',5-trimethoxybibenzyl and 3',4-dihydroxy-3,4',5-trimethoxybibenzyl were reported only from the genus *Dendrobium* [8,9], and it could be used as a chemotaxonomic marker to differentiate *Dendrobium* from other species of Orchidaceae. 4',5-Dihydroxy-3,3'-dimethoxybibenzyl was reported from the

genera *Dendrobium* [10,17], *Bletilla* [18], and *Pholidota* [19] of Orchidaceae. 7-Hydroxy-2,8-dimethoxy-1,4-diphenanthraquinone was only reported from the genera *Dendrobium* [11] and *Cypripedium* [20] of Orchidaceae. 7-Hydroxy-2-methoxy-1,4-diphenanthraquinone was only reported from the genera *Dendrobium* [12,21] and *Bletilla* [22] of Orchidaceae. 2,4-Di-tert-butyl phenol ether was dimer phenol derivate with unusual di-tert-butyl substituent. To the best of our knowledge, these have only been identified from the genera *Dendrobium* [23], *Bletilla* [24], *Pholidota* [25] of Orchidaceae. These bibenzyl and diphenanthraquinones compounds could be used as potential chemotaxonomic markers for species of Orchidaceae. *β*-Sitosterol occurs extensively in plant kingdom, and it's of little chemotaxonomic value.

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Supporting Information

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