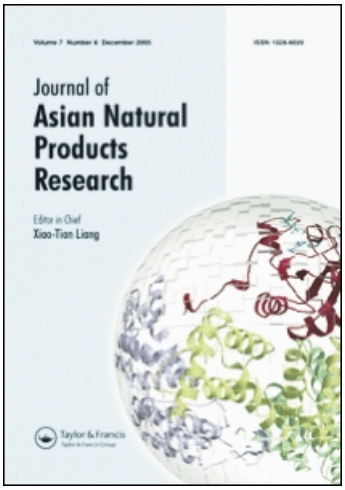

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Two new stilbenoids, 9-(4′-hydroxy-3′-methoxyphenyl)-10-(hydroxymethyl)-11-methoxy-5,6,9,10-tetrahydrophenanthro[2,3-*b*]furan-3-ol (**1**) and 2-(4″-hydroxybenzyl)-3-(3′-hydroxyphenethyl)-5-methoxy-cyclohexa-2,5-diene-1,4-dione (**2**), together with the three known stilbenoids were isolated from the tubers of *Pleione bulbocodioides* (Franch.) Rolfe. Their structures were elucidated by spectroscopic methods.

Keywords: *Pleione bulbocodioides*; stilbenoids; phenanthrofuran; bibenzyl

1. Introduction

The tubers of *Pleione bulbocodioides* (Franch.) Rolfe have been used in Chinese medicine as anticancer and antibacterial agents. A number of stilbenoids have been isolated from *P. bulbocodioides* [1,2] and various biological activities, such as antimicrobial and antiallergic activities have been reported [3,4]. During our search for anticancer compounds from Chinese herbal medicine, we investigated the constituents of *P. bulbocodioides*, which led to the isolation of two new stilbenoids, 9-(4′-hydroxy-3′-methoxyphenyl)-10-(hydroxymethyl)-11-methoxy-5,6,9,10-tetrahydrophenanthro[2,3-*b*]furan-3-ol (**1**) and 2-(4″-hydroxybenzyl)-3-(3′-hydroxyphenethyl)-5-methoxy-cyclohexa-2,5-diene-1,4-dione (**2**), together with the three known stilbenoids **3**, **4**, and **5**. Herein, we describe the structural determination of compounds **1** and **2**.

2. Results and discussion

An ethanolic extract of the tubers of *P. bulbocodioides* was partitioned with petroleum ether, EtOAc, and *n*-BuOH, successively. The EtOAc part was repeatedly subjected to column chromatography to yield two new stilbenoids **1** and **2**, and three known stilbenoids **3**, **4**, and **5**.

Compound **1** was obtained as amorphous powder. Its molecular formula $C_{25}H_{24}O_6$ was determined based on the quasi-molecular ion peak $[M-H]^-$ at *m/z* 419.1498 in the HR-ESI-MS spectrum. The IR spectrum revealed absorption bands of hydroxy (3319 cm^{-1}) and aromatic rings (1602 and 1436 cm^{-1}). The ^1H NMR spectrum of **1** (Table 1) showed signals characteristic of a dihydrophenanthrene skeleton [one multiplet ethylene group at δ 2.68 (4H, m, H-5, 6), three aromatic protons as an ABX system at δ 6.65 (1H, m, H-2), 6.67 (1H, d, $J = 2.5$ Hz, H-4), and 8.00 (1H, d, $J = 9.0$ Hz, H-1), and a singlet at δ 6.54 (1H, s, H-7)] [5], a 4′-hydroxy-3′-methoxyphenyl group [three aromatic protons as an ABX system at δ 6.76 (1H, d, $J = 8.5$ Hz, H-5′), 6.83 (1H, dd, $J = 8.5$, 2.0 Hz, H-6′), and 6.93 (1H, d, $J = 2.0$ Hz, H-2′)], two methines at δ 5.61 (1H, d, $J = 4.5$ Hz, H-9),

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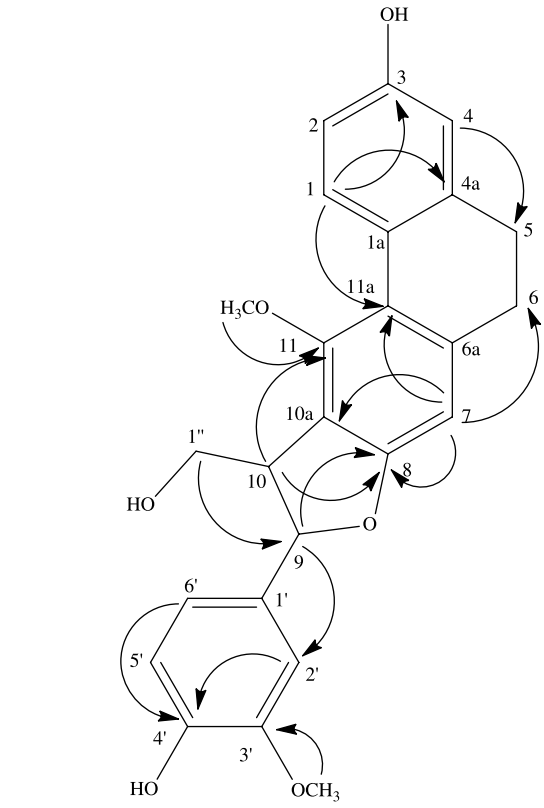
Table 1. ^{1}H and ^{13}C NMR spectral data and HMBC correlations of compound **1** (^{1}H, 500 MHz; ^{13}C, 125 MHz; in CD_3OD).

	δ_H	δ_C	HMBC
1	8.00 (d, 9.0)	128.0	H-1/C-3, 4a, 11a
2	6.65 (m)	113.1	
3	–	155.6	
4	6.67 (d, 2.5)	114.0	H-4/C-1a, 2, 5
5	2.68 (m)	29.9	
6	2.68 (m)	30.8	
7	6.54 (s)	104.9	H-7/C-6, 8, 10a, 11a
8	–	159.6	
9	5.61 (d, 4.5)	87.5	H-9/C-1′, 2′, 6′, 8, 10a, 1″
10	3.64 (m)	53.3	H-10/C-8, 11
11	–	155.2	
1a	–	124.6	
4a	–	139.5	
6a	–	141.8	
10a	–	117.3	
11a	–	120.3	
1′	–	134.2	
2′	6.93 (d, 2.0)	109.1	H-2′/C-4′, 6′
3′	–	147.9	
4′	–	146.2	
5′	6.76 (d, 8.5)	115.0	H-5′/C-3′, 1′
6′	6.83 (dd, 8.5, 2.0)	118.1	H-6′/C-2′, 4′
1″	4.06 (dd, 11.0, 4.0)	62.9	H-1″/C-9, 10
	3.73 (m)		
11-OCH_3	3.57 (s)	59.1	H-CH_2O/C-11
3′-OCH_3	3.82 (s)	55.2	H-CH_2O/C-3′

3.64 (1H, m, H-10), and an oxygenated methylene at δ 4.06 (1H, dd, $J = 11.0, 4.0$ Hz, H-1″), 3.73 (1H, m, H-1″), as well as two methoxyl group at δ 3.82 (3H, s) and 3.57 (3H, s). The ^{13}C NMR spectrum (Table 1) combined with HSQC experiment exhibited signals for 25 carbons including one ethylene, one oxygenated methylene, two methoxyls, and two methines, one of which was oxygenated, along with 18 aromatic carbons (seven protonated carbons, six quaternary carbons, and five oxygenated carbons). In the HMBC spectrum (Figure 1), the correlations of H-10 (δ 3.64) to C-8 and C-11 and H-9 (δ 5.61) to C-8, C-10a, C-1′, and C-1″ revealed that C-8, C-9, C-10, and C-10a formed a furan skeleton with an oxygen. The correlations of H-1″ (δ 4.06) to C-9 and C-10 indicated C-1″ was linked to C-10. The correlations of H-9 (δ 5.61) to C-2′ and C-6′; H-6′ (δ 6.83), H-2′ (δ 6.93) to C-4′ (δ 146.2), and the methoxyl (δ 3.82) to C-3′ (δ 147.9) indicated the presence of the 4′-hydroxy-3′-methoxyphenyl group that was linked to C-9. Another methoxyl (δ 3.57) was linked to C-11 because of its correlation to C-11 of the dihydrophenanthrene skeleton. The other ^{1}H and ^{13}C signals could be attributed by analyses of the HMBC and HSQC spectra (Table 1 and Figure 1). Therefore, the structure of **1** was elucidated as 9-(4′-hydroxy-3′-methoxyphenyl)-10-(hydroxymethyl)-11-methoxy-5,6,9,10-tetrahydrophenanthro[2,3-*b*]furan-3-ol.

Compound **2** was obtained as yellow crystals (MeOH). Its molecular formula $C_{22}H_{20}O_5$ was determined based on the quasi-molecular ion peak $[M+Na]^+$ at *m/z* 387.1207 in the HR-ESI-MS spectrum. The IR spectrum revealed absorption bands of hydroxy (3213 cm^{-1}), carbonyl (1716 cm^{-1}), and aromatic (1602, 1510, and



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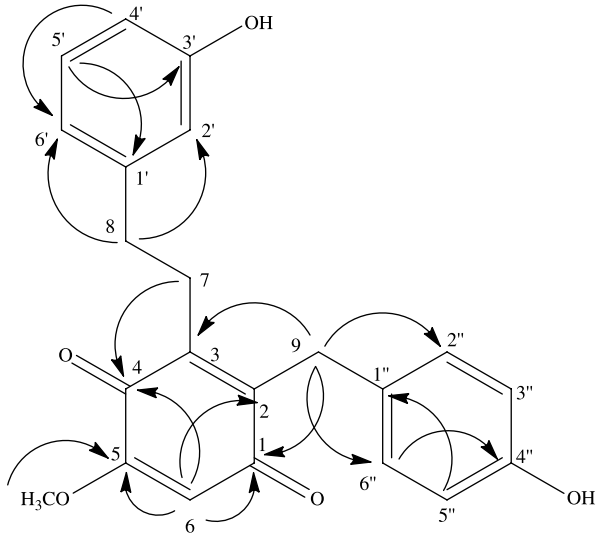

2

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

1456 cm^{-1}) rings. The ^1H NMR spectrum of **2** (Table 2) showed signals of a *p*-hydroxyphenyl group [four aromatic protons as an AA′BB′ system at δ 6.93 (2H, brd, $J = 8.5$ Hz, H-2″, H-6″) and 6.75 (2H, brd, $J = 8.5$ Hz, H-3″, H-5″)], a 3′-hydroxyphenyl group [four aromatic protons at δ 7.06 (1H, t, $J = 8.0$ Hz, H-5′), 6.62 (1H, m, H-4′), 6.59 (1H, m, H-2′), and 6.58 (1H, m, H-6′)] [6], one methoxyl group at δ 3.83 (3H, s), one ethylene at δ 2.75 (2H, m, H-7), 2.46 (2H, m, H-8), one methylene at δ 3.63 (2H, s, H-9), and an aromatic proton at δ 6.02 (1H, s, H-6). The ^{13}C NMR spectrum (Table 2) combined with HSQC experiment exhibited the signals for 22 carbons. Six of them (δ 189.1, 145.3, 143.4, 184.0, 160.1, and 108.0) were similar to the signals of a *p*-benzoquinone skeleton [7], and the other 16 carbons consisted of one ethylene, one methylene, one methoxyl, and 12 unsaturated carbons (eight protonated carbons, two quaternary carbons, and two oxygenated carbons), which were consistent with the assumption of the two phenyl group. In the HMBC spectrum (Figure 1), the clear correlations of H-6 (δ 6.02) to C-1, C-2, C-4, and C-5; H-7 (δ 2.75) to C-2, C-3, and C-4; H-9 (δ 3.63) to C-1, C-2, and C-3; and H-8 (δ 2.46) to C-3 confirmed that C-1, C-2, C-3, C-4, C-5, and C-6 formed a *p*-benzoquinone skeleton, and C-3 was linked to C-7 and C-2 was linked to C-9. The correlations of H-8 (δ 2.46) to C-2′, C-6′ indicated that the 3′-hydroxyphenyl group was linked to C-8. The correlations of H-9 (δ 3.63) to C-2″, C-6″ indicated that the *p*-hydroxyphenyl group was linked to C-9. The methoxyl (δ 3.83) was linked to C-5 because of its correlation to C-5 of the *p*-benzoquinone skeleton. The other ^1H and ^{13}C signals could be attributed by the analyses of the HMBC and HSQC spectra (Table 2 and Figure 1). Therefore, the structure of **2** was elucidated as 2-(4″-hydroxybenzyl)-3-(3′-hydroxyphenethyl)-5-methoxy-cyclohexa-2,5-diene-1,4-dione.

Compounds **3**, **4**, and **5** were elucidated as shanciol F, batatansin III, gymconopin D,

Table 2. ^1H and ^{13}C NMR spectral data and HMBC correlations of compound **2** (^1H, 500 MHz; ^{13}C, 125 MHz; in CD_3OD).

	δ_H	δ_C	HMBC
1		189.1	
2		145.3	
3		143.4	
4		184.0	
5		160.1	
6	6.02 (s)	108.0	H-6/C-1, 2, 4, 5
7	2.75 (m)	30.2	H-7/C-1′, 2, 3, 4
8	2.46 (m)	35.6	H-8/C-3, 7, 2′, 6′
9	3.63 (s)	31.2	H-9/C-1, 2, 3, 2″, 6″
1′		144.0	
2′	6.59 (m)	116.3	H-2′/C-8, 4′, 6′
3′		158.5	
4′	6.62 (m)	114.1	H-4′/C-2′, 6′
5′	7.06 (t, 8.0)	130.4	H-5′/C-3′, 1′
6′	6.58 (m)	120.7	H-6′/C-8, 4′
1″		130.8	
2″	6.93 (brd, 8.5)	130.5	H-2″/C-9, 4″
3″	6.75 (brd, 8.5)	116.4	H-3″/C-5″, 1″
4″		156.9	
5″	6.75 (brd, 8.5)	116.4	H-5″/C-3″, 1″
6″	6.93 (brd, 8.5)	130.5	H-6″/C-9, 4″
OCH_3	3.83 (s)	56.8	H/C-5

respectively, by the comparison of the spectroscopic data with those reported in the literature [2,4,8]. It should be noted that compound **5** was isolated from this species for the first time.

3. Experimental

3.1 General experimental procedures

Optical rotations were recorded on a PE 241 MC polarimeter. The IR spectra were recorded on a Bio-Rad FTS 6000 infrared spectrometer. The UV spectra were measured on a Shimadzu UV-2450 spectrophotometer. The NMR spectra were run on Bruker AVANCE-400 and Varian unity INOVA-500 spectrometers, using TMS as an internal standard. Mass spectra were obtained on an IonSpec 7.0T FTMS instrument. Preparative HPLC was carried out on an ODS column (250 × 20 mm i.d., YMC) with a JASCO RI-1530 intelligent refractive index detector. Silica gel (200–300 mesh, Qingdao Ocean Chemical Group Co., Qingdao, China) and Sephadex LH-20 (Merck Co., Darmstadt, Germany) for column chromatography as well as silica gel GF254 (Qingdao Ocean Chemical Group Co.) for TLC were used.

3.2 Plant material

The tubers of *P. bulbocodioides* were purchased from Anguo Meiwei Material Medica Cooperation in Hebei Province, China in August 2005. The plant was identified by Prof. Wen-Yuan Gao, School of Pharmaceutical Science and Technology, Tianjin University. A voucher specimen (No. 20050801) has been deposited at School of Pharmaceutical Science and Technology, Tianjin University.

3.3 Extraction and isolation

The tubers of *P. bulbocodioides* (30 kg) were extracted thrice with 95% EtOH under reflux for 3 h. After the removal of solvent under reduced pressure, the extract was suspended in water and partitioned with petroleum ether, EtOAc, and *n*-BuOH, successively. The EtOAc-soluble part (500 g) was subjected to column chromatography over silica gel eluting with petroleum ether–EtOAc to EtOAc–MeOH gradient system with increasing amounts of EtOAc and MeOH, respectively, to give seven fractions. Fraction 6 was rechromatographed over a silica gel column eluting with $CHCl_3$–MeOH (95:5, 9:1, 85:15) to yield three subfractions. The first and second subfractions were further fractionated on a Sephadex LH-20 column ($CHCl_3$–MeOH, 1:1) and then purified by preparative HPLC column to afford compounds **1** (8 mg), **2** (11 mg), **3** (15 mg), **4** (13 mg), and **5** (15 mg).

3.3.1 Compound **1**

Amorphous powder, $C_{25}H_{24}O_6$; $[\alpha]_D^{25}$ −5.82 ($c = 0.1$, MeOH). UV (MeOH) λ_{max} (log ε): 251 (4.17), 281 (4.32), and 308 (4.02) nm; IR (KBr) ν_{max} (cm^{-1}): 3319, 1602, and 1436; ^1H NMR (CD_3OD, 500 MHz) and ^{13}C NMR (CD_3OD, 125 MHz) spectral data: see Table 1; HR-ESI-MS (negative) *m/z*: 419.1498 $[M-H]^-$ (calcd for $C_{25}H_{23}O_6$, 419.1495).

3.3.2 Compound **2**

Yellow crystals (MeOH), $C_{22}H_{20}O_5$; UV (MeOH) λ_{max} (log ε): 221 (4.12) and 274 (3.81) nm; IR (KBr) ν_{max} (cm^{-1}): 3213, 1716, 1602, 1510, and 1456. ^1H NMR (CD_3OD, 500 MHz) and ^{13}C NMR (CD_3OD, 125 MHz) spectral data: see Table 2; HR-ESI-MS (positive) *m/z*: 387.1207 $[M+Na]^+$ (calcd for $C_{22}H_{20}O_5$ Na, 387.1208).

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