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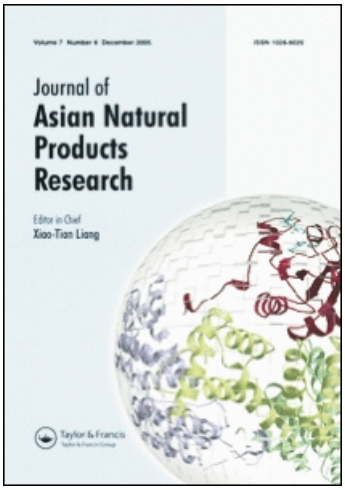

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Stilbenoids from *Stemona sessilifolia*

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Two new dihydrostilbenes, stilbostemins H (**1**), I (**2**), and a new dihydrophenanthrene, stemanthrene E (**3**), were isolated and identified from the roots of *Stemona sessilifolia*, together with known stilbostemins B, D and G, and stemanthrenes A and C (**4**–**8**). Structures of new stilbenoids were established by 1D and 2D ^{1}H NMR and ^{13}C NMR spectroscopic analyses.

Keywords: *Stemona sessilifolia*; Stilbenoids; Stilbostemins H-I; Stemanthrene E

1. Introduction

The genus *Stemona* contains about 25 species, among which *S. sessilifolia*, *S. japonica* and *S. tuberosa* have long been prescribed in traditional Chinese medicine as insecticides and antitussive agents [1–3]. Up to now, extracts from roots of these three species are still used to treat respiratory disorders, including pulmonary tuberculosis and bronchitis, and externally used against different insect pests [4–6]. In our previous study on several *Stemona* species in China, many alkaloids were isolated and structurally identified [7–13]. Antibacterial and antifungal stilbenoids were also isolated from the ethanol extract of *S. tuberosa* [14]. Recently a series of antifungal stilbenoids were revealed from the chloroform extract of *S. collinsae* and *S.* cf. *pierrei* [15,16], and some of these stilbenoids also exhibited bioactivities of inhibiting leukotriene biosynthesis [17]. In our further investigation on the chemical components from *S. sessilifolia,* three new stilbenoids were isolated and purified from the roots of the title plant with five known compounds. By comparison with the previously published data [14,16], the known compounds were identified as stilbostemin B (**4**), stilbostemin D (**5**), stilbostemin G (**6**), stemanthrene A (**7**) and stemanthrene C (**8**).

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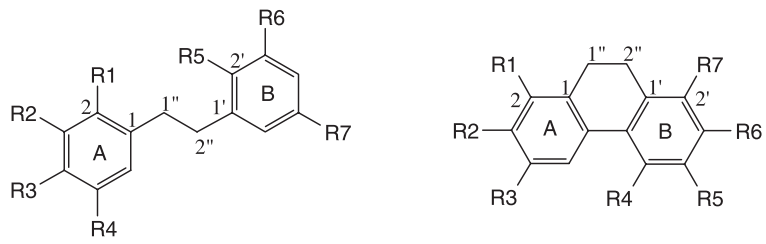
2. Results and discussion

Stilbostemin H (**1**) was obtained as colourless crystals. The molecular formula of **1** was established as $C_{17}H_{20}O_4$ on the basis of the HREI-MS ([M] $^+$, *m/z* 288.1364), which was in agreement with the EI-MS and ^{13}C NMR data. The ^{1}H NMR spectrum (table 1) showed signals attributable to one 1,2,5-trisubstituted benzene, one 1,3,5-trisubstituted benzene, three methoxyl groups, and one hydroxyl group, as well as two methylenes, indicating **1** to be a tetrasubstituted bibenzyl. To determine the substituted positions of the methoxyl and hydroxyl groups, ROESY and HMBC experiments (figures 2 and 3) were carried out. Strong NOE correlations between a methoxyl signal at δ_H 3.80 and H-3 and H-1″ and between the hydroxyl signal and H-4 and H-6 revealed that these two substituted groups were in position 2 and 5, respectively. Thus the remaining positions of 3′ and 5′ should be substituted by two other methoxyl groups. HMBC experiments provided further evidences for the substituted positions. The correlations were observed between the signals of 5-OH and C-4 and C-6, and between H-4, H-6 and H-1″ and C-2, which proved a 2-methoxy-5-hydroxy substitution in ring A. The 3′,5′-dimethoxy substitution of ring B was confirmed by the symmetry proton signals and coupling constants in the 1,3,5-trisubstituted benzene. Moreover, the presence of two fragment ions at *m/z* 137 ($C_8H_9O_2$) and 151 ($C_9H_{11}O_2$) in the EI-MS spectrum also proved the substituted patterns in two aromatic rings. The ^{1}H NMR and ^{13}C NMR data were assigned in table 1 by ROESY and HMBC experiments. Thus, **1** was identified as 1-(2-methoxy-5-hydroxyphenyl)-2-(3,5-dimethoxyphenyl)-ethane (figure 1).

Stilbostemin I (**2**) was isolated as colourless crystals and assigned the molecular formula of $C_{18}H_{22}O_3$ by HREI-MS and ^{13}C NMR data. The ^{1}H NMR spectrum (table 1) showed signals attributable to four aromatic protons in one 1,2-disubstituted benzene moiety, two equivalent aromatic proton singlets in the other benzene moiety, three methoxyl groups, and one methyl group, as well as two methylenes, indicating **2** to be a tetrasubstituted bibenzyl. Meanwhile, the ^{13}C NMR spectrum exhibited four signals in aromatic region (δ_C 140.9, 103.8, 158.0, 111.6), which suggested one aromatic moiety (ring A) was symmetrically substituted as 3,5-dimethoxy-4-methyl or 2,6-dimethoxy-4-methylbenzyl. This was confirmed by the presence of two fragment ions at *m/z* 121 (C_8H_9O) and 165 ($C_{10}H_{13}O_2$) in the EI-MS spectrum. NOE correlations between one methoxyl signal at δ_H 3.88 and H-3′ and H-2″ and between two methoxyl signals at δ_H 3.85 and H-2, 4-methyl and H-6 revealed



1 R_1,R_6,R_7=OMe, R_2,R_3,R_5=H, R_4=OH
2 R_1,R_6,R_7=H, R_2,R_4,R_5=OMe, R_3=Me
3 R_1,R_5,R_7=H, R_2,R_4=OH, R_3=Me, R_6=OMe
4 R_1,R_5,R_6,R_7=H, R_2,R_4=OH, R_3=Me
5 R_1,R_6,R_7=H, R_2,R_4=OH, R_3=Me, R_5=OMe
6 R_1,R_7=H, R_2,R_6=OH, R_3=Me, R_4,R_5=OMe
7 R_1,R_4=OMe, R_2,R_6=OH, R_3,R7=H, R_5=Me
8 R_1,R_4=OMe, R_2,R_6=OH, R_3=H, R_5,R_7=Me

Figure 1. Structures of **1**–**8**.

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Table 1. ^{1}H and ^{13}C NMR data for **1**–**3** in $CDCl_3$ (δ in ppm, J in Hz).

No.	*^{1}H NMR*			*^{13}C NMR*		
	1	***2***	***3***	***1***	***2***	***3***
1				129.8	140.9	137.7
2		6.36 s	6.70 s	152.2	103.8	114.8
3	6.73 d (8.0)			111.6	158.0	151.9
4	6.64 dd (8.0, 2.2)			113.2	111.6	121.4
5			7.79 s	149.4	158.0	128.2
6	6.62 d (2.2)	6.36 s		117.3	103.8	125.7
1′				144.0	130.2	141.2
2′	6.37 m		6.42 d (2.4)	106.8	157.4	106.5
3′		6.86 brd (7.7)		161.2	110.2	158.6
4′	6.32 dd (2.4, 2.4)	7.23 ddd (7.8, 7.7, 1.7)	6.35 d (2.4)	98.2	127.1	100.7
5′		6.87 m		161.2	120.3	153.2
6′	6.37 m	7.15 m		106.8	129.9	114.5
1″	2.84 m	2.85 m	2.67 m	33.7	35.9	29.4
2″	2.79 m	2.91 m	2.69 m	37.4	31.9	30.7
2-OMe	3.80 s			55.8		
3-OMe		3.85 s			55.7	
4-Me		2.04 s	2.28 s		7.9	15.8
5-OH/OMe	4.76 s	3.85 s			55.7	
2′-OMe		3.88 s			55.3	
3′-OMe	3.76 s		3.79 s	55.6		55.3
5′-OMe	3.76 s			55.6		

that three methoxyl groups were in position 2′, 3 and 5, respectively. HMBC experiments (figure 3) provided more evidences to elucidate the structure of **2**. These findings led to a conclusion that **2** had the structure as 1-(3,5-dimethoxy-4-methylphenyl)-2-(2-methoxy phenyl)-ethane.

Stemanthrene E (**3**) was found to possess the molecular formula of $C_{16}H_{16}O_3$ by HREI-MS, ^{13}C NMR spectra (table 1), consistent with nine degrees of unsaturation. Compared with the above stilbostemins, **3 s**howed more intense UV absorption bands at 302

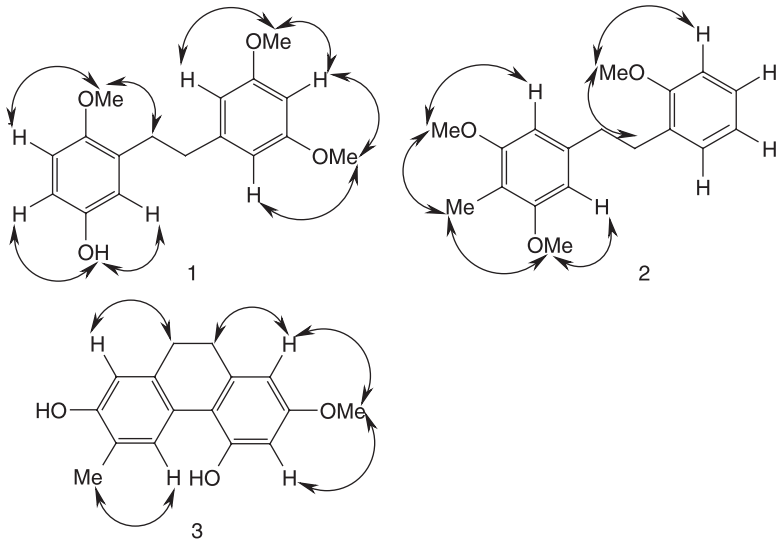

Figure 2. Key ROESY correlations for **1**–**3**.

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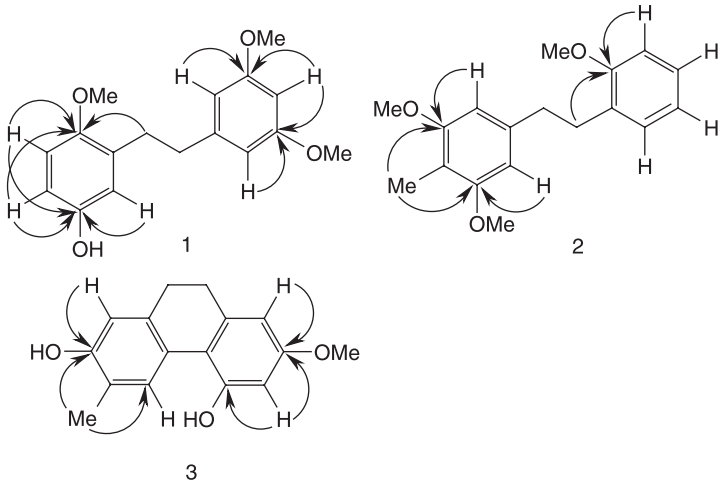

Figure 3. Selective HMBC correlations for **1**–**3** (H to C).

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and 216 nm, which were typical for dihydrophenanthrenes [15–16]. The ^{13}C NMR and DEPT spectra (table 1) displayed 16 carbons and 14 C-bonded proton signals correlated to two benzene rings, one methoxyl group, one methyl, and two methylenes. Supported by ROESY experiments (figure 2), the positions of the substituted groups were determined. The NOE contacting chain H-2″ ↔ H-2′ ↔ 3′-OCH_3 ↔ H-4′ allowed the assignment of two meta coupling protons in ring B. Thus the remaining two singlet protons should be in ring A. The correlation between one proton at δ_H 6.70 and H-1″ revealed it was attached to C-2 and the other one should be in position 5. The cross peak between the methyl signal at δ_H 2.28 and H-5 showed it was in position 4. The remaining positions 3 and 5′ should be substituted by two hydroxys. Therefore the structure of **3** was identified as a dihydrophenanthrene with one methoxyl group at C-3′, two hydroxyl groups at C-3 and C-5′ and one methyl group at C-4, respectively. Moreover, HMBC experiments (figure 3) confirmed this substitution pattern and also allowed the assignment of the ^{13}C resonances. As a result, the structure of **3** was determined to be 2,5-dihydroxy-7-methoxy-3-methyl-9,10-dihydrophenanthrene.

3. Experimental

3.1 General experimental procedures

All melting points were determined on a Fisher-Johns melting point apparatus and were uncorrected. The UV spectra were detected on a Hewlett-Packard 8452A diode array spectrophotometer. IR spectra were recorded on a Nicolet Magna 750 FTIR (KBr) spectrophotometer. All MS data were obtained with MAT-95 mass spectrometer. NMR spectra were recorded on a Bruker AM-400 instrument with TMS as internal standard, the chemical shift values are reported in unit (δ) and coupling constants (J) were given in Hz. Silica gel (100–200, 200–300 mesh) and silica gel (GF_{254}) for precoated plates (produced by Qingdao Haiyang Chemical Group Co., Qingdao, China) were used for column chromatography and for preparative TLC, respectively.

3.2 Plant material

The fresh roots of *Stemona sessilifolia* were collected in Tuzhou County, Anhui Province, P.R. China, in September 2002, and identified by Professor Jin-gui Shen of Shanghai Institute of Materia Medica, Chinese Academy of Sciences. A voucher specimen (20020014B) was deposited in the Herbarium of the institute.

3.3 Extraction and isolation

Air-dried roots of *S. sessilifolia* (10 kg) were ground and then percolated with 95% EtOH. The concentrated extract was suspended in MeOH/H_2O and partitioned successively with petroleum ether, chloroform, EtOAc and n-BuOH. The $CHCl_3$-soluble fraction (55 g) was subjected to the column chromatography over silica gel eluting with petroleum ether/acetone gradients (4:1 – 1:2). The evaporated residue from petroleum ether/acetone (3:1) elution was subjected to repeated chromatography on silica gel with 20% EtOAc in hexane, which led to 15 mg of **2**. The evaporated residue from petroleum ether/acetone (2:1) elution was re-chromatographed on Sephadex LH-20 with 1 L MeOH in 100 fractions, combined according to TLC comparison. Crystallisation of the combined fractions 12 – 35 and 38 – 50 in Et_2O led to 250 mg of **4** and 150 mg of **5**, respectively. Preparative TLC of the combined fractions 51 – 55 afforded **6** (4 mg), **7** (9 mg), and **8** (4 mg) with 25% EtOAc in hexane. The combined fractions 56 – 95 eluted with 15% EtOAc in hexane over silica gel column afforded 120 mg of impure **1** and 75 mg of impure **3**. Further purification of **1** and **3** by recrystallisation in acetone led to 87 mg and 45 mg of pure compounds, respectively.

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3.4 Identification

3.4.1 Stilbostemin H (1). Colourless crystals; mp 79°C; UV (MeOH) λ_{max} (log ε) (nm): 281 (3.45), 214 (4.05); IR (KBr) ν_{max} (cm^{-1}): 3251, 2956, 2833, 1610, 1591, 1502, 1469, 1436, 1319, 1220, 1149, 1070, 1029, 937, 867, 694; EI-MS *m/z*: 288 $[M]^+$(75), 272 (8), 257 (22), 241 (5), 223 (10), 205 (9), 197 (7), 181 (10), 165 (12), 151 (92), 149 (85), 137 (100), 121 (40), 107 (38), 91 (37), 77 (34), 57 (59); HREI-MS *m/z*: 288.1364 $[M]^+$ (calcd for $C_{17}H_{20}O_4$, 288.1362); ^1H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) data: see table 1. ROESY: 2-OCH_3 ↔ H-1″, H-3 ↔ 2-OCH_3, 5-OH ↔ H-4, H-6 ↔ 5-OH, H-1″ ↔ H-6, H-1″ ↔ H-2″, H-2″ ↔ H-2′, H-2′ ↔ 3′-OCH_3, 3′-OCH_3 ↔ H-4′, H-4′ ↔ 5′-OCH_3, 5′-OCH_3 ↔ H-6′, H-6′ ↔ H-2″. HMBC (H → C): 2-OCH_3 → 2; H-3 → 1, 2, 5; H-4 → 2, 3, 5, 6; 5-OH → 4, 5, 6; H-6 → 1″, 2, 4; H-2′ → 2″, 3′, 4′; H-6′ → 2″, 4′, 5′; 3′-OCH_3 → 3′; H-4′ → 2′, 6′; 5′-OCH_3 → 5′; H-1″ → 1, 2, 6, 1′, 2″; H-2″ → 1, 1′, 2′, 6′, 1″.

3.4.2 Stilbostemin I (2). Colourless crystals; mp 72 – 74°C; UV (MeOH) λ_{max} (log ε) (nm): 270 (3.49), 204 (4.25); IR (KBr) ν_{max} (cm^{-1}): 3004, 2954, 2836, 1608, 1589, 1494, 1465, 1419, 1322, 1242, 1180, 1137, 1033, 759, 605; EI-MS *m/z*: 286 $[M]^+$(20), 165 (100), 150 (11), 135 (9), 121 (72), 105 (8), 91 (45), 77 (13); HREI-MS *m/z*: 286.1563 $[M]^+$ (calcd for $C_{18}H_{22}O_3$, 286.1569); ^1H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) data see table 1. ROESY: H-1″ ↔ H-2, H-2 ↔ 3-OMe, 3-OMe ↔ 4-Me, 4-Me ↔ 5-OMe, 5-OMe ↔ H-6, H-6 ↔ H-1″, H-1″ ↔ H-2″, H-2″ ↔ 2′-OMe, 2′-OMe ↔ H-3′, H-6′ ↔ H-2″. HMBC (H → C): H-2 → 1″, 3, 4, 6; 3-OMe → 3; 4-Me → 3, 4, 5; 5-OMe → 5; H-6 → 1″, 2,

4, 5; H-1″ → 2, 6, 1′, 2″; H-2″ → 1, 2′, 6′, 1″; 2′-OMe → 2′; H-3′ → 1′, 5′; H-4′ → 2′, 6′; H-5′ → 1′, 3′; H-6′ → 2′, 4′, 2″.

3.4.3 Stemanthrene E (3). Colourless crystal; mp 163–165°C; UV (MeOH) λ_{max} (log ε) (nm): 302 (3.1), 277 (3.9), 216 (4.2); IR (KBr) ν_{max} (cm^{-1}): 3388, 2927, 1616, 1594, 1503, 1459, 1438, 1411, 1305, 1228, 1194, 1060, 862; EI-MS *m/z*: 256 $[M]^+$(100), 241 (57), 227 (5), 212 (6), 195 (7), 181 (6), 165 (6), 152 (7), 128 (8), 115 (5), 91(3), 76 (6); HREI-MS *m/z*: 256.1097 $[M]^+$ (calcd for $C_{16}H_{16}O_3$, 256.1099); ^1H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) data: see table 1. ROESY: H-1″ ↔ H-2, 4-CH_3 ↔ H-5, H-1″ ↔ H-2″, H-2″ ↔ H-2′, H-2′ ↔ 3′-OCH_3, 3′-OCH_3 ↔ H-4′. HMBC (H → C): H-2 → 3, 4, 6, 1″; 4-CH_3 → 3, 4, 5; H-5 → 1, 3, 6′; H-2′ → 2″, 3′, 4′, 6′; 3′-OCH_3 → 3′; H-4′ → 2′, 3′, 5′, 6′; H-1″ → 1, 2, 6, 1′, 2″; H-2″ → 1, 1′, 2′, 6′, 1″.

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