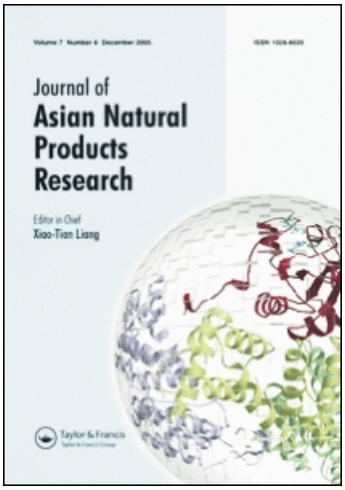

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PYRROLE ALKALOIDS FROM *BOLBOSTEMMA PANICULATUM*

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Three pyrrole alkaloids were isolated from *Bolbostemma paniculatum*. Their structures were elucidated as 4-(2-formyl-5-methoxymethylpyrrol-1-yl)butyric acid methyl ester (**1**), 2-(2-formyl-5-methoxymethylpyrrol-1-yl)-3-phenylpropionic acid methyl ester (**2**) and α-methyl pyrrole ketone (**3**) by spectroscopic techniques. Among them, **1** and **2** are new compounds.

Keywords: *Bolbostemma paniculatum*; Pyrrole alkaloids

INTRODUCTION

The bulbs of *Bolbostemma paniculatum* (Maxim.) Franquet are a Chinese folk medicine named "Tu Bei Mu" which is often used for the treatment of tumors as well as for detoxication. Previous research indicated that the main constituents in this plant are triterpenoid saponins, which have anticancer bioactivity [1,2]. It has not been reported that alkaloids have been isolated from this plant. We report here the isolation and structural elucidation of one known and two new pyrrole alkaloids from bulbs of *Bolbostemma paniculatum* (Maxim.) Franquet.

RESULTS AND DISCUSSION

The MeOH extract of the dried and powdered bulbs was successively partitioned with light petroleum, $CHCl_3$ and *n*-BuOH. The chloroform fraction was chromatographed on silica gel, Sephadex LH20 and finally on reversed-phase silica gel to afford compounds **1**, **2** and **3** (Fig. 1).

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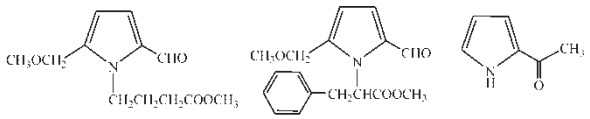

1 2 3

FIGURE 1 Structures of compounds **1**, **2** and **3**.

Compound **1** was isolated as a yellow oil with molecular formula $C_{12}H_{17}NO_4$ deduced from HREIMS spectrum (see Experimental). The IR spectrum of **1** revealed the presence of two carbonyls, one for ester (1739 cm^{-1}) and one for aldehyde (1667 cm^{-1}). The ^{13}C NMR and DEPT spectra of **1** (See Table I) showed the presence of two methoxyl groups (δ 52.11 and 58.21), four methylenes (δ 27.49, 31.66, 45.80, and 66.34), three methines (δ 112.91, 125.89 and 181.11) as well as three quaternary carbons (δ 133.89, 141.07 and 175.07). The presence of two double bonds was confirmed by the two methines at δ 112.91 and 125.89 together with the two quaternary carbon signals at δ 133.89 and 141.07. The other methine signal at δ 181.11 indicated the presence of an aldehyde group adjacent to the double bond.

The ^1H NMR spectrum exhibited the presence of signals at δ 2.35 (2H, t, $J = 7.2$ Hz), 2.00 (2H, m), 4.36 (2H, m) and 4.48 (2H, s) assignable to the methylene protons H-2, H-3, H-4 and H-7′ respectively. The proton signals at δ 3.65 and 3.34 (each 3H, s) corresponded to the methyl group of the ester functionality at C-1 and the methoxyl groups at C-7′ respectively. The proton signal at δ 9.34 (1H, s) was assignable to the aldehyde group located at C-2′. It also showed two proton doublets at δ 6.97 (1H, d, $J = 4.0$ Hz) and δ 6.28 (1H, d, $J = 4.0$ Hz) for H-3′ and H-4′, which revealed the attachment of the two double bonds.

The HMQC spectra analysis of **1** assigned significantly the correlations between each carbon and its directly linked protons while the interpretation of the proton–proton couplings were established by $^1H-^1H$ COSY measurements. The HMBC spectral analysis of **1** displayed correlation peaks between H-5 with C-1, H-2 with C-1, C-3 and C-4, H-4 with C-2, C-3, C-2′ and C-5′, H-6′ with C-2′, H-7′ with C-8′ and C-5′ (see Fig. 2). The presence of a pyrrole ring moiety was further confirmed by the HMBC correlations between H-4 with both C-2′ and C-5′, in accordance with the formula of **1** and Ref. [3].

Consequently, **1** is identified as 4-(2-formyl-5-methoxymethylpyrrol-1-yl)butyric acid methyl ester.

Compound **2** was also isolated as a yellow oil. Its molecular formula was determined as $C_{17}H_{19}NO_4$ by HREIMS spectral analysis (See Experimental). Its IR spectrum revealed the presence of two carbonyl groups (1744, 1667 cm^1). Comparison of the ^1H NMR and ^{13}C NMR spectra of **2** (See Table II) with that of **1** also indicated the presence of a 2-formyl-5-methoxymethylpyrrole fragment in **2**. In addition, the presence of

TABLE I NMR data of compound **1** (CD_3OD, 400 MHz)

No.	δ_H (J_{Hz})	δ_C	*No.*	δ_H (J_{Hz})	δ_C
1		175.07	2′		133.89
2	2.35 (2H, t, *J*=7.2)	31.66	3′	6.97 (1H, d, *J*=4.0)	125.89
3	2.00 (2H, m)	27.49	4′	6.28 (1H, d, *J*=4.0)	112.91
4	4.36 (2H, m)	45.80	5′		141.07
5	3.65 (3H, s)	52.11	6′	9.34 (1H, s)	181.11
			7′	4.48 (2H, s)	66.34
			8′	3.34 (3H, s)	58.21

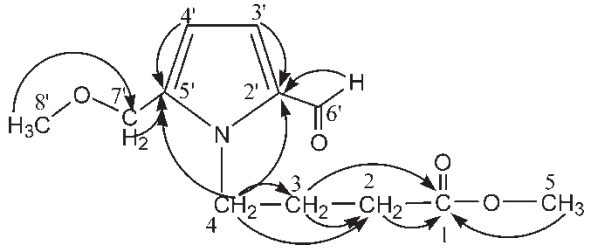

FIGURE 2 Significant HMBC correlations for compound **1**.

a mono-substituted aromatic ring, one methylene, one methine, one ester-carbonyl, as well as one methoxyl group was also observed in ^{1}H and ^{13}C NMR spectra of **2**. The HMBC spectrum displayed correlation peaks between H-2 with C-1 (ester-carbonyl), C-2′ and C-5′ (pyrrole ring), H-3 with C-2, C-5 and C-9 (aromatic ring) (see Fig. 3). Therefore, **2** is identified as 2-(2-formyl-5-methoxymethylpyrrol-1-yl)-3-phenylpropionic acid methyl ester.

EXPERIMENTAL

General Experimental Procedures

IR data were obtained with a Bruker Vector-22 instrument. NMR spectra were acquired on a Varian INOVA-400, with TMS as internal standard. EI-MS data were obtained on a Varian Mat-212, by the direct inlet method. Chromatographic column: silica gel H (10−40μ, Qing Dao Oceanic Chemical Industry), Sephadex LH20 (Pharmacia), C_{18} (25−40μ, Merck). All other chemical solvents were analytically pure.

Plant Material

The bulbs of *Bolbostemma paniculatum* (Maxim.) Franquet were collected at Shanxi Province, China and identified by Dr Chen Wan-sheng, Department of Pharmacognosy, School of Pharmacy, Second Military Medical University, Shanghai, China, where a voucher specimen has been deposited.

Extraction and Isolation

The dried and powdered bulbs (50 kg) were extracted with cool MeOH by infiltration. After removal of the solvents by evaporation under reduced pressure, the extract was suspended in

TABLE II NMR data of compound **2** (CD_3OD, 400 MHz)

No.	δ_H (J_{Hz})	δ_C	*No.*	δ_H (J_{Hz})	δ_C
1		171.26	2′		133.94
2	5.34 (1H, br)	62.36	3′	7.10 (1H, d, *J*=4)	127.59
3	3.24 (1H, dd, *J*=11.4,14)	38.91	4′	6.11 (1H, d, *J*=4)	112.32
	3.66 (1H, dd, *J*=3.6,14)		5′		142.52
10	3.70 (3H, s)	52.94	6′	9.42 (1H, s)	180.74
4		139.00	7′	3.60 (1H, d, *J*=13.2)	66.35
5 and 9	6.84 (2H, m)	130.19		3.84 (1H, d, *J*=13.2)	
6 and 8	7.14 (3H, m)	129.53	8′	3.08 (3H, s)	57.80
7		127.90			

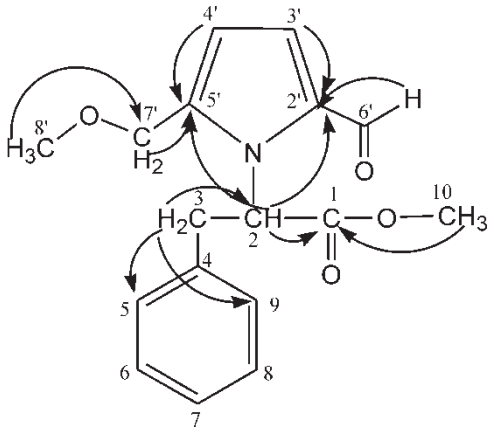

FIGURE 3 Significant HMBC correlations for compound **2**.

water and then partitioned with light petroleum, $CHCl_3$ and *n*-BuOH successively. The chloroform fraction (245 g) was chromatographed on silica gel (9 × 100 cm), eluting with light petroleum containing gradually increasing amounts of acetone to give fractions 1–33.

Fraction 9 (12 g) was chromatographed on silica gel (5 × 40 cm), with light petroleum–acetone (40:1) as eluent to yield 7 fractions. The fifth fraction was chromatographed repeatedly on a column of Sephadex LH20 (2 × 80 cm) with MeOH as eluent and finally yielded compound **3** (30 mg).

Fraction 12 (8 g) was chromatographed on silica gel (5 × 40 cm), with light petroleum–acetone (10:1) as eluent to yield 4 fractions. Fraction two (1 g) was chromatographed on silica gel (2 × 20 cm), eluting with light petroleum–acetone (20:1) to give two fractions, of which the second fraction was a mixture of compounds **1** and **2**. The mixture was chromatographed on a column of reversed-phase silica gel (2 × 30 cm), eluting with 60% MeOH (H_2O). This afforded compounds **1** (24 mg) and **2** (4 mg).

Structure and Identification

Compound **1**, $C_{12}H_{17}NO_4$, yellow oil; IR (KBr) ν_{max}: 3118, 2930, 2824, 1739, 1667 (C═O), 1453, 1366, 1197, 1094, 1038, 904, 780 cm^{-1}; ^1H NMR and ^{13}C NMR data, see Table I; HREI-MS [239.1164 (calc. 239.1158)]; EI-MS *m/z*: 239 $[M]^+$ (69), 225 (61), 210 (100), 196 (48), 180 (23), 178 (22), 164 (27), 150 (34), 134 (78), 120 (9), 108 (23), 106 (23), 101 (29).

Compound **2**, $C_{17}H_{19}NO_4$, yellow oil; IR (KBr) ν_{max}: 3062, 3028, 2929, 2825, 2730, 1744, 1667 (C═O), 1451, 1243, 1090, 1040, 903, 754, 702 cm^{-1}; ^1H NMR and ^{13}C NMR data, see Table II; HREI-MS [301.1319 (calc. 301.1314)]; EI-MS *m/z*: 301 $[M]^+$ (100), 283 (17), 272 (40), 270 (31), 269 (64), 242 (21), 210 (42), 198 (6), 178 (25), 167 (11), 150 (10), 139 (58), 138 (33), 131 (36), 103 (14), 91[*ph*-CH_2-]$^+$ (25).

Compound **3**, C_6H_7NO, yellow needles; mp 63–65°C; IR (KBr) ν_{max}: 3275(NH), 1755 (C═O), 1655, 1548 (C═C), 1497, 1464, 1405, 1322, 1191, 1045 cm^{-1}; ^1H NMR($CDCl_3$) δ: 2.468 (3H, s, CH_3), 6.295 (1H, m, 4-H), 6.950 (1H, m, 3-H), 7.080 (1H, m, 5-H), 10.159 (1H, br, s, NH); ^{13}C NMR ($CDCl_3$) δ: 25.288 (CH_3), 110.498 (4-C), 116.924 (3-C), 124.889 (5-C), 132.216 (2-C), 188.034 (C═O); EI-MS *m/z*: 109 $[M]^+$ (24), 94$[M - CH_3]^+$ (56), 88 (14), 86 (100), 84 (39), 66$[M - CH_3CO]^+$ (5). The ^1H NMR and ^{13}C NMR data mentioned above are in accord with that in Ref. [3].

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