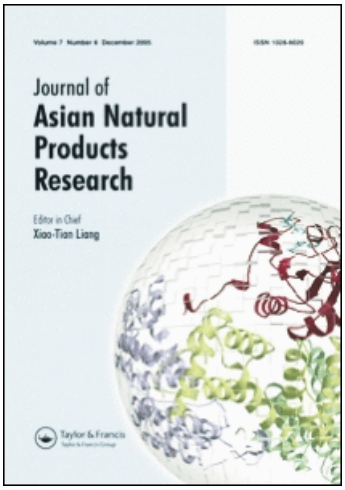

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Stemoninine-type alkaloids from the roots of *Stemona sessilifolia*

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Two new stemoninine-type alkaloids, stemoninine A (**1**) and B (**2**), along with two known *Stemona* alkaloids, bisdehydrostemoninine (**3**) and bisdehydrostemoninine A (**4**), were isolated from the roots of *Stemona sessilifolia*, and their structures and relative configurations were determined on the basis of spectrometric data analysis.

Keywords: Alkaloids; Stemoninine A; Stemoninine B; *Stemona sessilifolia*

1. Introduction

The roots of *Stemona sessilifolia* Miq. (Stemonaceae), named "Bai Bu" in traditional Chinese herb medicine, have been used as an antitussive agent and insecticide in China for a long time. Phytochemical studies of Stemonaceae plants have been focused thus far on *Stemona* alkaloids, and more than 90 alkaloids have been reported in the literature.[1] We have previously reported four sessilistemonamine-type alkaloids, with a novel tetracyclic skeleton derived from pyrrolo[1,2-α]azepine, isolated from the roots of *S. sessilifolia*.[2,3] In our further studies on the constituents of *S. sessilifolia*, two new stemoninine-type alkaloids, named stemoninines A (**1**) and B (**2**), along with two known *Stemona* alkaloids, bisdehydrostemoninine (**3**) and bisdehydrostemoninine A (**4**),[4] were isolated from an ethanolic extract of the roots of *S. sessilifolia*. Here we report the isolation and characterization of the four compounds (Figure 1).

2. Results and discussion

Compound **1** was obtained as yellow gum. Its molecular formula was determined as $C_{22}H_{29}O_5N$ (*m/z* 387.2037 $[M]^+$) on the basis of HREI–MS. EI–MS showed the molecular ion at *m/z* 387 and a strong fragment ion peak at *m/z* 343 $[M - CO_2]^+$. The ^{13}C NMR and DEPT spectra of **1** showed 22 carbon atoms, including five quarternary, eight methine, six methylene and three methyl carbons. The low-field carbonyl carbons at δ 178.9, combined with the strong IR absorption bond at 1763 cm^{-1}, suggested the presence of lactone moieties. The ^1H NMR spectrum of **1** showed three methyl groups at δ 1.35 (d, $J = 7.0$ Hz, Me-22), 1.30 (d, $J = 7.0$ Hz, Me-15) and 1.06 (t, $J = 7.5$ Hz, Me-17); two olefinic protons at δ 6.12 (d, $J = 3.5$ Hz, H-2) and 5.88 (d, $J = 3.5$ Hz, H-1); two CH groups next to an *O*-atom and a CH_2 group next to a *N*-atom at δ 5.38 (dd, $J = 5.5$, 11.0 Hz, H-18), 3.55 (td, $J = 10.0$, 3.5 Hz, H-8), 4.26 (dd, $J = 5.5$, 14.0 Hz, H-5α) and 3.73 (dd, $J = 11.0$, 14.0 Hz, H-5β).

A spin system involving H-18, H-19, H-20 and H-22 in the $^1H-^1H$ COSY experiment, coupled with the correlations between H-22 and C-21; H-20 and C-21 in the HMBC spectrum, revealed the presence of a lactone moiety comprising C-18, C-19, C-20, C-21 and C-22, which was determined to be localised at C-3 by the long-range correlations between H-18 and C-2, C-3 in the HMBC experiment. Another lactone moiety was determined by the $^1H-^1H$ correlations between H-15, H-13 and H-12 in the $^1H-^1H$ COSY spectrum, as well as the long-range correlations between H-15 and C-12, C-13 and C-14; H-12 and C-11 in the HMBC spectrum. It was determined to be connected with C-10 by the long-range correlations between H-10 and C-11; H-12 and C-10. The C-11 was determined to be a spiro-atom connected to two oxygen atoms by the chemical shift at δ_C 113.9 in the ^{13}C NMR spectrum. Therefore, the evidence revealed that **1** contained a basic skeleton of stemoninines.[5] By comparison of its ^1H NMR and ^{13}C NMR spectra with those of stemoninines,[6] **1** has a saturated ring D and a dehydroazaazulene ring (rings A and B). The $^1H-^1H$ COSY and key HMBC correlations of **1** are shown in Figure 2.

The relative configuration of **1** was revealed by NOE difference spectrum coupled with the software package of CambridgeSoft Chem3D (see Figure 3). According to a conventional β orientation of H-18 in most of *Stemona* alkaloids[1], the correlation of H-18 with H-20 indicated the β-orientation of H-20. Because of the chair-conformation of the seven-membered ring B, H-5α

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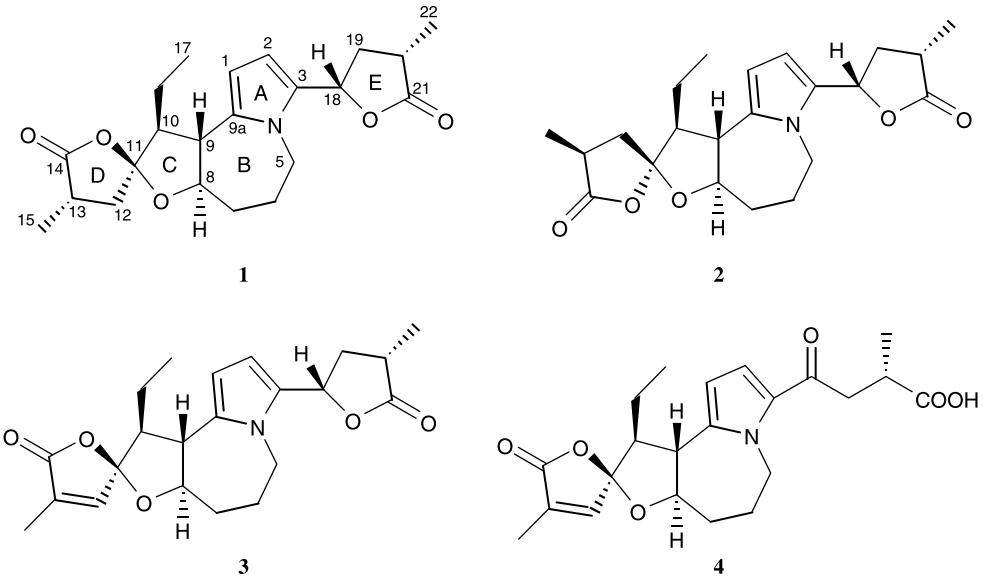


Figure 1. Structures of compounds **1**–**4**.

showed a NOE correlation with H-18. The H-9 was confirmed with a β-orientation by its correlation with H-5β. The facts of no NOE correlation between H-9 and H-8, and a visible correlation between H-8 and H-10 revealed the α-orientation of both H-8 and H-10. The configuration of C-11 was determined by the fact that no NOE correlation was observed between H-9 and H-12. The α-orientation of H-15 was deduced by a weak NOE correlation between H-15 and H-17.

Compound **2** was obtained as colourless prisms. Its molecular formula was determined as $C_{22}H_{29}O_5N$, identical to that of **1**, on the basis of HREI–MS (*m/z* 387.2068 $[M]^+$). Careful analysis of spectrometric data resulted in the conclusion that **2** was a stereoisomer of **1**. The relative configuration of **2** was revealed by NOE difference spectrum coupled with the software package of CambridgeSoft Chem3D. Configurations of C-8, C-9, C-10, C-18 and C-20 proved to be identical to those of **1**. The key NOE correlations are shown in Figure 3. The configuration of C-11 was determined to be contrary to that of **1** by the facts that a correlation between H-9 and H-12 could be observed and no correlation was observed between H-10 and H-12. The β-orientation of H-15 was revealed by the fact that no NOE correlation was observed between H-15 and H-17.

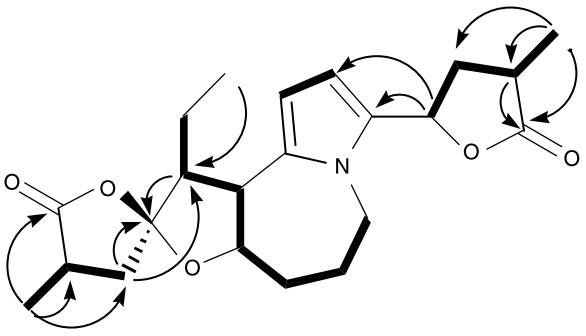


Figure 2. $^1H-^1H$ correlations (bold lines) and key HMBC correlations of **1**.

Compounds **3** and **4** were identified as bisdehydrostemoninine and bisdehydrostemoninine A, respectively, by comparison of their NMR spectroscopic data with those in the literature, which were isolated from *Stemona tuberose*[4]. However, the mp 180–181°C and $[\alpha]_D^{20}$ − 125°($c = 0.11$, MeOH) values of **3** are quite different from those reported in the literature.

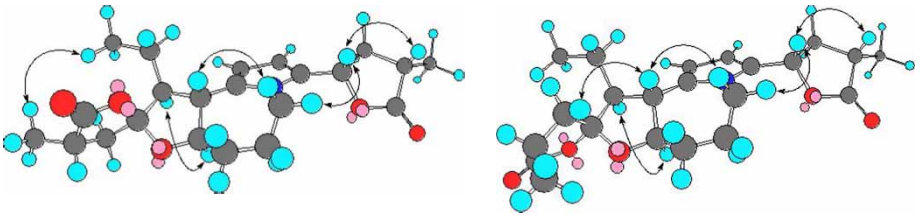
3. Experimental

3.1 General experimental procedures

Melting points were measured on a XT_4-100 × microscopic melting point apparatus and are uncorrected. Optical rotations were determined on a Perkin–Elmer 343 digital polarimeter. IR spectra were obtained on a Nicolet IMPACT-400 FT-IR spectrometer. EI–MS and HREI–MS spectra were recorded on an Autospec-UltimaETOF mass spectrometer. NMR spectra were recorded on an INOVA 500 NMR spectrometer. In ^1H NMR spectra, the chemical shifts are given in δ (ppm) relative to the resonances of $CHCl_3$ at δ 7.26. In ^{13}C NMR spectra, the chemical shifts are given in δ (ppm) relative to the resonances of $CHCl_3$ at δ 77.0.

3.2 Plant material

The roots of *Stemona sessilifolia* were obtained from Ding Xian market, Hebei Province, China, in June 2005.



1 2

Figure 3. Key NOE correlations of compounds **1** and **2**.

The plant material was identified by Professor Lin Ma of the Institute of Materia Medica. A voucher specimen (No. pc337-07) has been deposited in the Department of Natural Medicinal Chemistry, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.

3.3 *Extraction and isolation*

The dried roots (24.4 kg) of *S. sessilifolia* were ground and extracted with 95% EtOH at reflux. After evaporation of the solvent, a dark residue was obtained, which was suspended in 85% aq. EtOH and extracted with petroleum ether (PE; bp 60–90°C) to remove lipophilic substances. The ethanolic phase was evaporated in vacuum, and the residue was partitioned between EtOAc and H_2O. The EtOAc phase was combined and evaporated *in vacuo* to give a residue (115 g), which was subjected to silica gel column chromatography using gradient elution from 100% $CHCl_3$ to 10% MeOH/$CHCl_3$. The fraction (41 g) eluted with $CHCl_3$ was further chromatographed on silica gel, eluting with a gradient petroleum ether/EtOAc to afford compounds **2** (9.5 mg), **3** (35.4 mg) and **4** (16.0 mg). The fraction (21 g) eluted with $CHCl_3$/MeOH (50:1) was further chromatographed on silica gel, eluting with a gradient petroleum ether/EtOAc to afford compound **1** (8.6 mg).

3.3.1 *Compound **1***

Yellow gum, $[\alpha]_D^{20}$ −88.3 (*c* 0.06, MeOH), IR ν_{max} (Microscope transmission) 2936, 1763, 1166, 965 cm^{-1}; ^1H NMR and ^{13}C NMR ($CDCl_3$) spectra data: see Table 1;

Table 1. ^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectral data for compounds **1** and **2** (δ in ppm, J in Hz, in $CDCl_3$).

Position	Stemoninine A (**1**)		Stemoninine B (**2**)	
	^1H	^{13}C	^1H	^{13}C
1	5.88 (d, $J = 3.5$)	103.0 (d)	5.94 (d, $J = 3.5$)	104.3 (d)
2	6.12 (d, $J = 3.5$)	106.8 (d)	6.12 (d, $J = 3.5$)	106.9 (d)
3		128.5 (s)		128.5 (s)
5	4.26 (dd, $J = 5.5, 14.0$, H_α) 3.73 (dd, $J = 11.0, 14.0$, H_β)	45.2 (t)	4.29 (dd, $J = 5.5, 14.0$, H_α) 3.70 (m, H_β)	45.4 (t)
6	2.05, 1.63 (each m, 1 H)	26.2 (t)	2.05, 1.62 (each m, 1 H)	25.9 (t)
7	2.27 (td, $J = 11.5, 3.5$, H_α) 1.72 (m, H_β)	35.5 (t)	2.33 (m, H_α) 1.60 (m, H_β)	34.4 (t)
8	3.55 (td, $J = 10.0, 3.5$)	83.4 (d)	3.67 (m)	80.9 (d)
9	3.13 (t, $J = 11.0$)	47.6 (d)	2.74 (t, $J = 10.0$)	49.8 (d)
9a		133.8 (s)		133.7 (s)
10	2.42 (m)	50.2 (d)	2.86 (dd, $J = 7.5, 9.5$)	50.1 (d)
11		113.9 (s)		115.0 (s)
12	2.48 (dd, $J = 8.5, 13.5$) 2.12 (t, $J = 13.5$)	40.7 (d)	2.35, 2.07 (each m, 1 H)	38.5 (d)
13	2.99 (m)	34.4 (d)	2.99 (m)	34.7 (d)
14		178.9 (s)		178.9 (s)
15	1.30 (d, $J = 7.0$)	15.2 (q)	1.29 (d, $J = 7.0$)	15.0 (q)
16	1.77 (m)	20.7 (t)	1.74, 1.58 (each m, 1 H)	23.6 (t)
17	1.06 (t, $J = 7.5$)	12.9 (q)	0.98 (t, $J = 7.5$)	12.3 (q)
18	5.38 (dd, $J = 5.5, 11.0$)	71.5 (d)	5.37 (dd, $J = 5.5, 11.0$)	71.7 (d)
19	2.70, 2.22 (each m, 1 H)	34.7 (t)	2.70, 2.22 (each m, 1 H)	34.7 (t)
20	2.80 (m)	36.0 (d)	2.80 (m)	36.0 (d)
21		178.9 (s)		178.9 (s)
22	1.35 (d, $J = 7.0$)	15.0 (q)	1.35 (d, $J = 7.0$)	14.9 (q)

HREI–MS *m/z* 387.2037 $[M]^+$ (calcd for $C_{22}H_{29}O_5N$, 387.2046), EI–MS *m/z* 388 (7, $[M + H]^+$), 387 (88, M^+), 358 (11), 343 (90), 340 (35), 218 (100), 174 (42), 172 (35).

3.3.2 Compound ***2***

Colourless prisms, mp 199–200°C, $[\alpha]_D^{20}$ 0 (*c* 0.06, MeOH), IR ν_{max} (Microscope transmission) 2932, 1753, 1161, 956 cm^{-1}; ^1H NMR and ^{13}C NMR ($CDCl_3$) spectra data: see Table 1; HREI–MS *m/z* 387.2068 $[M]^+$ (calcd for $C_{22}H_{29}O_5N$, 387.2046), EI–MS *m/z* 388 (24, $[M + H]^+$), 387 (100, M^+), 358 (25), 343 (85), 218 (98), 174 (37), 172 (20).

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