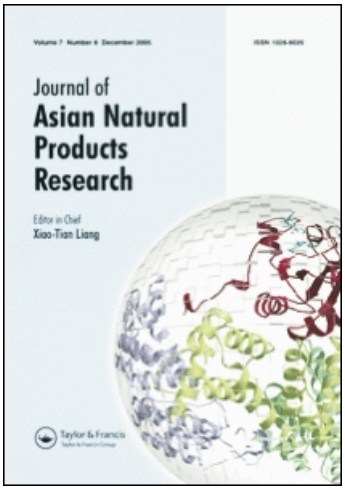

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CHINESE BITTERSWEET ALKALOID III, A NEW COMPOUND FROM *CELASTRUS ANGULATUS*

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A novel skeleton alkaloid named Chinese Bittersweet Alkaloid III from the leaves of *C. angulatus* was reported. The structure and its stereochemistry were established by IR, 1D and 2DNMR (^{1}H-^{1}HCOSY, HMQC, HMBC, NOESY), MS and elemental analysis.

Keywords: Bittersweet alkaloid; *Calastrus angulatus*; Structural elucidation

INTRODUCTION

Previously we have reported the isolation and structure elucidation of two new alkaloids (Chinese bittersweet alkaloids I and II) from the leaves of *Celastrus angulatus* [1]. Further investigation of the plant leaves has led to the isolation of another new alkaloid. The structure of the alkaloid (Scheme 1) has been established by spectroscopic analysis as 6α,9α-dimethyl, 5α-ethyl, 8α-propyl, 4β-formyl, 8β-acetoxy, N^3-ethyl-piperidino[1,2-a]piperazine (Chinese bittersweet alkaloid III). The structure of the alkaloid is similar to marfortime A isolated by Lee and Polonsky *et al.* [2–3] and paraherquamide A isolated by Yamaki *et al.* [4]. We report here the isolation and structure of this new alkaloid.

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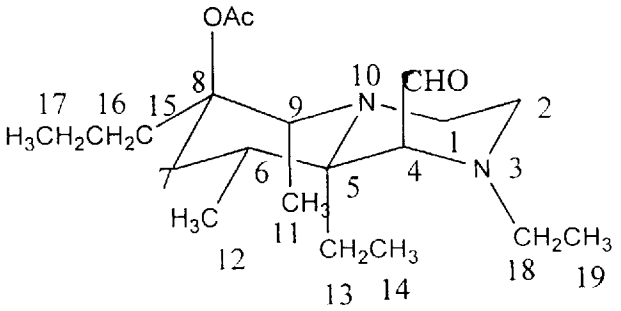


SCHEME 1

RESULTS AND DISCUSSION

The alkaloid is a yellow-oil with easy deliquescence in air. Its taste is bitter and pungent. Positive Dragendorff test indicated the feature of alkaloid properties. IR absorptions showed the presence of C—N bond (3230, 2750–2250 br.s, 1650, 1550 cm^{-1}), aliphatic aldehyde group (2715 and 1730 cm^{-1}) and ester carbonyl group at 1715 cm^{-1}. EIMS ($[M]^+$ 352) and elemental analysis (C: 68.54%, H: 10.74%, N: 7.45%) established the molecular formula to be $C_{20}H_{36}O_3N_2$, which was also supported by ^{1}HNMR, ^{13}CNMR and DEPT data.

The ^{13}CNMR (DEPT) data (Tab. I) of the compound displayed 20 carbon signals including six methyls, seven methylenes, three methines, two quaternary carbons (of which one was joined with oxygen, and the other joined with nitrogen), an ester carbonyl carbon and an aldehyde group carbon. The ^{1}H-^{1}HCOSY and HMQC spectra revealed the following partial structural units of $—CH_2CH_3$, $—CH_2CH_2CH_3$, $>NCH_2CH_3$, $>NCH_2CH_2N<$, $>NCHCHO$, $>NCHCH_3$, $>CHCH_3$, $CH_3COO—$ and $>CH—CH_2—C<$. The two geminal protons of the last mentioned methylene have unequal chemical shifts. The element composition of the compound was deduced combining EIMS $[M]^+$ at m/z 352 with elemental analysis results. According to the molecular formula the alkaloid contained four unsaturation equivalents. Beside the two carbonyls there was no evidence for other unsaturation signals in NMR. The above facts indicated that the alkaloid must be a bicyclic system. All possible structural candidates of the alkaloid are shown in Scheme 2.

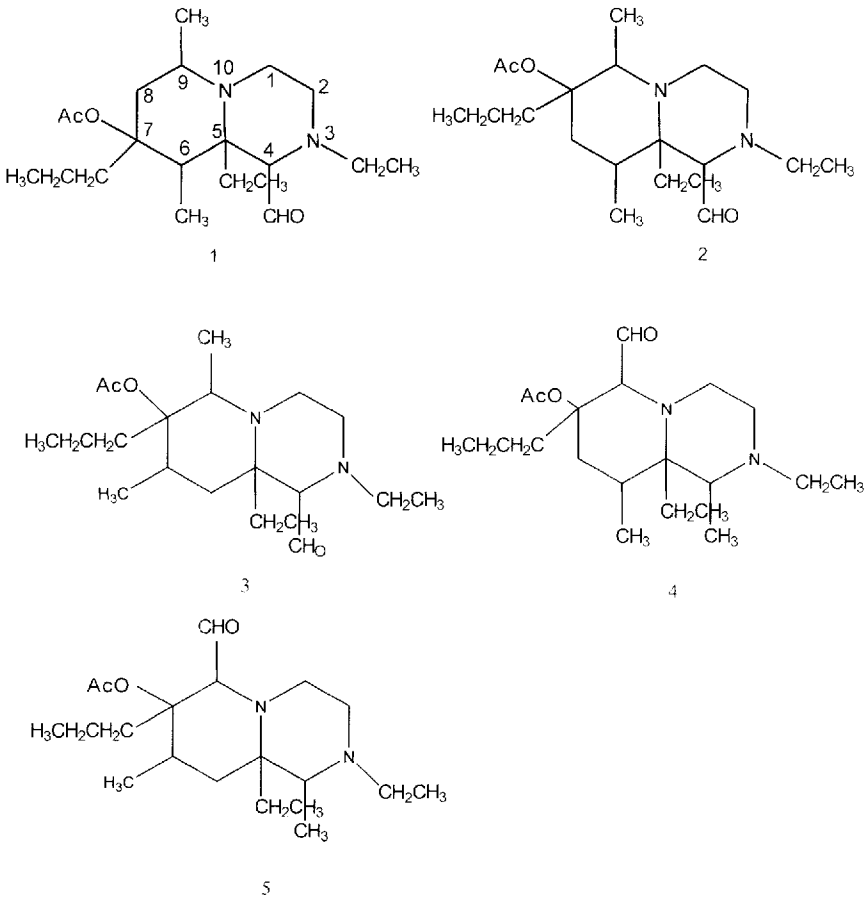
The ^{1}HNMR spectrum showed a multiplet at δ 3.20 which can only be assigned to H-9 from ^{1}H-^{1}HCOSY according to structure 1 and δ_H 3.20 was

TABLE I ^{1}H-, ^{13}CNMR data in DMSO-d_6 of the alkaloid III

	Correlated hydrogen		*Correlated carbon*		
Position	δ_H *(ppm)*	^{1}H-$^{1}HCOSY$	*HMQC (ppm)*	*DEPT*	*HMBC*
1	2.95 m	H-1/H-2	48.6	CH_2	
2	3.18 m	H-2/H-1	49.2	CH_2	
4	4.26 d	H-4/CHO	48.6	CH	
5			50.7	C	C-5/H-12
6	3.20	H-6/H-12	43.1	CH	C-6/H-12
7	1.79 m	H-7a/H-7e			
	2.04 m	H-7a/H-6	30.5	CH_2	
		H-7e/H-6			
8			63.3	C	C-8/H-11
9	2.95 m	H-9/H-11	49.8	CH	C-9/H-11
11	1.05 d	H-11/H-9	17.6	CH_3	
12	1.18 d	H-12/H-6	20.6	CH_3	
13	2.79 q	H-13/H-14	34.1	CH_2	C-13/H-14
14	1.14 t	H-14/H-13	12.8	CH_3	C-14/H-13
15	2.70 t	H-15/H-16	40.1	CH_2	C-15/H-16, H-17
16	1.56 m	H-16/H-15, H-17	21.1	CH_2	C-16/H-15, H-17
17	0.89 t	H-17/H-16	11.1	CH_3	C-17/H-15, H-16
18	3.20 m	H-18/H-19	43.0	CH_2	
19	1.77 t	H-19/H-18	20.6	CH_3	C-19/H-18
—CHO —H	8.60 d	CHO/H-4	166.0	CH	
—OAC —CH_3	1.83 s		22.7	CH_3	
			169.4	C	

in turn correlated with δ 1.79, δ 2.04. However, HMQC spectrum showed the signal at δ 3.20 was significantly correlated with the carbon signal at δ 43.1 which cannot be assigned to the CH connected to N atom, so the signal of δ 3.20 must be either H-6 or H-7. Thus the possible structure of the alkaloid should be either 2 or 4. The HMBC spectrum revealed that the carbon signal at δ 63.3 was correlated with the proton signal at δ 1.05, but not δ 1.18 and the carbon signal at δ 50.7 was correlated with the proton signal at δ 1.18 but not 1.05. In addition, HMBC spectrum indicated the other correlated signals at δ_C 49.8 with δ_H 1.05, δ_C 34.1 with δ_H 1.14, δ_C 40.1 with δ_H 1.56, δ_H 0.89, in agreement with structure 2. According to EIMS, the presence of a fragment ion peak at m/z 142 $[CH_3CH{=}C(OCOCH_3)CH_2CH_2CH_3]^+$ proved that the propyl group was substituted on C-8, but not C-5.

The stereochemistry of the alkaloid was established by the use of the proton coupling constant and NOESY experiments. On the basis of NOESY spectrum, the correlation of signals at δ 1.83 and 8.60 revealed that —OAc and —CHO were on the same side of the ring, *i.e.*, β-configuration. The correlations of signals at δ 1.05 and 0.89, 1.05 and 1.14, 1.18 and 1.14



SCHEME 2 The possible structures of the alkaloid.

showed that —CH_3(C-11), —CH_3(C-12), —CH_2CH_3, and —CH_2—CH_2—CH_3 were on the same side of the ring, *i.e.*, α-configuration (see Fig. 2). The $W_{(1/2)}$ value of H-6 at δ 3.20 was more than 10 Hz (11.6 Hz), which showed the H-6 must be axial supporting the above conclusion. From the Dreiding model, we could see that H-6 was axial-H, with lower field chemical shift (3.20 ppm), possibly affected by the two flanking carbonyl groups. The NOESY correlation of the alkaloid is summarized in Figure 2. The unambiguous assignment of the proton and carbon data are listed in Table I. Therefore, the structure of this bitter alkaloid was concluded as 6α, 9α-dimethyl, 5α-ethyl, 8α-propyl, 4β-formyl, 8β-acetoxy, N^3-ethyl-piperidino [1,2-a]piperazine.

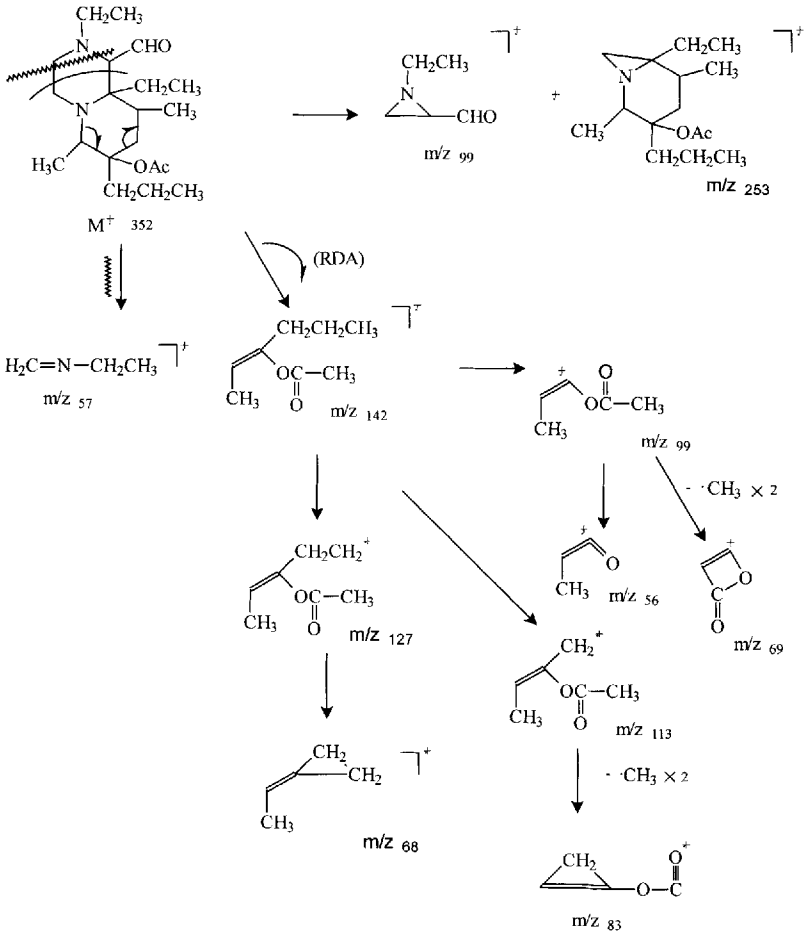


FIGURE 1 Proposed mass spectral fragmentation of the alkaloid III.

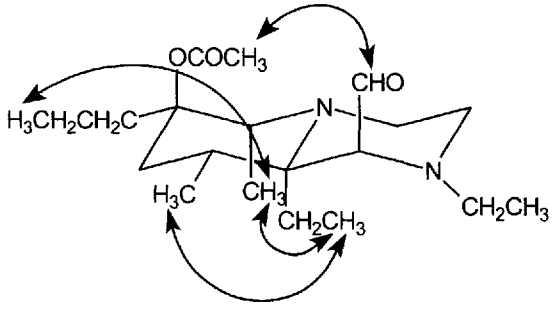


FIGURE 2 NOESY correlations used to establish the relative stereochemistry of the alkaloid indicated by double headed arrows.

EXPERIMENTAL SECTION

General Experimental Procedures

UV spectra were recorded on a Shimadzu UV-2100 spectrophotometer. IR spectra were recorded on a Perkin-Elmer 580B spectrometer. ^{1}H NMR, ^{13}C NMR (DEPT) and 2D correlation spectra were obtained on Bruker DPX-400 or 100 MHz NMR spectrometer, using DMSO-d_6 as solvent and TMS as internal standard. Mass spectra were measured on a HP5859 spectrometer and optical rotations were measured on a perkin-Elmer 341 Automatic Polarimeter, elemental analysis were carried out on a Perkin-Elmer240C Instrument.

Plant Material

The leaves and seeds of *C. angulatus* were collected in the Song shan county, Henan Province, in October 1996, and taxonomically authenticated by Prof. Chang-Shan Zhu, the Department of Botany Henan Agriculture University. A voucher specimen has been deposited in the Laboratory of Natural Products, Institute of Chemistry, Henan Academy of Sciences.

Extraction and Isolation

The air-dried leaves and seeds of *C. angulatus* (1 kg) were powdered and extracted with petroleum ether (2 × 5L) at room temperature, and the solvent was removed *in vacuo*. The residue was diluted with 500 ml H_2O. The soln was extracted with EtOAc. The EtOAc fraction was dried over Na_2SO_4 and concd. to dryness. The EtOAc extract was separated on a silica gel column, eluted by cyclohexane-EtOAc(2 : 8) to 17–21 frs, which were combined to give a yellow paste (75 mg). Dissolved in hot MeOH, the product was further purified by means of filtration and concentration to give the alkaloid (43 mg).

Chinese bittersweet alkaloid III (6α,9α-dimethyl, 5α-ethyl, 8α-propyl, 4β-formyl, 8β-acetoxy, N^3-ethyl-piperidino[1,2-a]piperazine), Yellow oil. [M]$^+$ 352, elemental analysis: C, 68.18%, H, 10.31%, N, 7.86%, calcd. for $C_{20}H_{36}O_3N_2$, Found: C, 68.54% H, 10.74% N, 7.45%. EIMS m/z 352, 253, 142, 127, 113, 69, 56; IR ν_{max} (cm)$^{-1}$: 3230, 2715–2250 (br. s), 1730, 1715, 1650, 1550, 1450, 1100, 1060; ^{1}HNMR (DMSO-d_6, 400 MHz): δ 0.89 (3 H, *t*, J = 7.6 Hz, H-17), 1.05 (3 H, *d*, J = 6.4 Hz, H-11), 1.14 (3 H, *t*, J = 7.6 Hz, H-14), 1.18 (3 H, *d*, J = 6.8 Hz, H-12), 1.56 (2 H, *m*, H-16),

1.77 (3 H, *t*, $>NCH_2CH_3$), 1.79 (1 H, *m*, H-7a), 1.83 (3 H, *s*, CH_3—CO—), 2.04(1 H, *m*, H-7e), 2.70 (2 H, *t*, $J = 7.6$ Hz, H-15), 2.79 (2 H, *q*, $J = 7.6$ Hz, H-13), 2.95 (1 H, *m*, H-9), 2.95 (2 H, *m*, H-1), 3.18 (2 H, *m*, H-2), 3.20 (1 H, br, H-6), 3.20 (2 H, *m*, H-18), 4.26 (1 H, *d*, $J = 5.2$ Hz, H-4), 8.60 (1 H, *d*, $J = 5.2$ Hz, —CHO). ^{13}CNMR (DMSO-d_6, 100 MHz) data see Table I.

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