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A NOVEL PYRROLIZIDINE ALKALOID FROM *LIGULARIA LANKONGENSIS*

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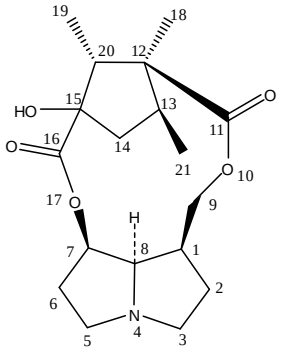
Abstract – A novel pyrrolizidine alkaloid named lankongensisine (**1**) was isolated from the roots of *Ligularia lankongensis*, and its structure was established by spectroscopic analysis.

Ligularia lankongensis is distributed in the southwest China and used as antitussive and expectorant agent in traditional Chinese medicine, but its chemical constituents have not been studied fully. In the previous study, we had isolated a few compounds from *L. lankongensis*.[1,2] This paper described the isolation and structure elucidation of a novel pyrrolizidine alkaloid named lankongensisine (**1**).



1

Compound (**1**) was determined to have the molecular formula of $C_{18}H_{27}NO_5$ by HREIMS (obsd.: 337.1881, calcd.: 337.1881). Eighteen signals in the ^{13}C NMR (DEPT) spectra were recognized as (4×C, 5×CH, 6×CH_2, 3×CH_3), of which the signals at 173.8 and 174.9 ppm indicated the presence of two ester carbonyl–carbons. In the ^1H NMR spectrum of **1,** two broad singlets at 5.01 and 3.59 ppm corresponded to two methine protons at C-7 and C-8; the signals of geminal methylene protons at C-9

appeared at 4.76 (J = 12.6, 5.3 Hz) and 3.97 ppm (J = 12.6 Hz). The two protons of H-9 had an appreciable differences of shift ($\delta_{H\text{-}9a}$- $\delta_{H\text{-}9b}$ = 0.79) and the coupling constant (J = 12.6 Hz), indicating that **1** was pyrrolizidine macrocylic diesters.[3,4] In the HMBC (**Figure 1**), the long-range correlation were observed between H-7 and C-16; H-9 and C-1, C-11; H-14 and C-13,C-15; H-18 and C-11, C-12, C-13, C-20; H-19 and C-12, C-13,C-14; H-20 and C-12, C-15, C-16; H-21 and C-12, C-15, C-20, respectively. The IR spectrum of **1** also showed characteristic signals for a free hydroxyl group at 3414 cm^{-1}. In the ^{13}C NMR, the chemical shift of δ84.4 (C-15) showed that free hydroxyl group connected at C-15. The relative configuration of **1** was derived from NOESY spectrum (**Figure 2**). Correlation were observed between H-1α and H-8α, H-9α, H-18; H-18 and H-13α, H-21; H-21 and H-7α, H-9α; H-7α and H-8α. Based on above analysis, the structure of this compound was identified as **1**, named Lankongensisine.

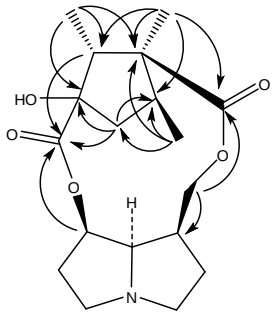


Figure 1. Selected HMBC of **1**

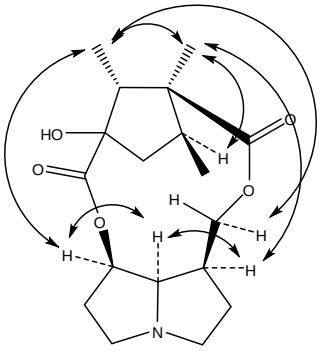


Figure 2. Selected NOESY of **1**

Table 1. The ^{1}H, ^{13}CNMR and HMBC Data of **1**[a]

No	^{1}H	^{13}C	HMBC
1	2.68 (1H, m)	40.8	C-2, C-7, C-8
2	2.07 (1H, m)	27.1	C-1, C-8
	1.74 (1H, m)		
3	3.15 (1H, m)	53.7	C-1, C-2, C-5, C-8
	2.85 (1H, m)		C-1, C-2, C-5, C-8
5	3.35 (1H, m)	52.9	C-3, C-6, C-7, C-8
	2.75 (1H, m)		C-3, C-6
6	2.25 (1H, m)	33.9	C-7, C-8
	2.20 (1H, m)		
7	5.01 (1H, brs)	77.3	C-5, C-16
8	3.59 (1H, brs)	70.0	C-1, C-2, C-3, C-7
9	4.76 (1H, dd, J = 12.6, 5.3)	60.8	C-1, C-8, C-11
	3.97 (1H, d, J = 12.6)		C-1, C-2, C-8, C-11
11	/	173.8	/

12	/	57.6	/
13	2.30 (1H, m)	43.1	C-11, C-12, C-14, C-18, C-19
14	2.75 (1H, m)	42.3	C-13, C-15, C-16, C-19
	2.10 (1H, m)		C-12, C-13, C-15, C-20
15	/	84.4	/
16	/	174.9	/
18	1.26 (3H, s)	22.4	C-11, C-12, C-13, C-20
19	1.02 (3H, d, J = 6.9)	14.2	C-12, C13, C-14
20	2.20 (1H, m)	60.9	C-12, C-15, C-16, C-18, C-21
21	0.87 (3H, d, J = 7.4)	11.0	C-12, C-15, C-20

[a] ^{1}H, ^{13}C NMR and 2DNMR spectra were obtained at 400MHz, 100MHz and 500MHz, and recorded in $CDCl_3$ at room temperature, respectively.

EXPERIMENTAL

General Experimental Procedures. Melting points were determined using a Kofler micro-melting point apparatus and are uncorrected. Optical rotations were determined on Horiba SEPA-300 polarimeter. IR spectra were obtained on KBr pellets using a Bio-Rad FTS-135 spectrophotometer. 1D and 2D NMR spectra were recorded on a Bruker AM-400 and Bruker DRX-500 spectrometers, respectively. EIMS and HREIMS measurements were carried out on a VG Auto Spec-3000 spectrometers.

Plant Material. The *Ligularia lankongensis* was collected in Lijiang, Yunnan Province, China in July 2000. A voucher specimen has been deposited in the Herbarium of China Pharmaceutical University.

Extraction and Isolation. The air-dried and powered root (20 kg) of *L. lankongensis* was extracted with 90% EtOH three times under reflux (each process lasting 3h). After removal of the solvent by evaporation, the residues were extracted with 0.8% H_2SO_4. The acid soluble fraction was defatted with $CHCl_3$, and then the acidic solution was reduced with zinc dust for 5h and filtered. The filtrate was made alkaline with ammonia and extracted with $CHCl_3$. The $CHCl_3$ solution was evaporated to give a crude alkaloidal mixture (15.0 g). The mixture was chromatographed over silica gel column using petroleum ether : acetone : diethylamine solvent system to afford lankongensisine (**1**) (25 mg).

Lankongensisine (**1**): yellow gum, $[\alpha]_D^{20}$ +51.4 (*c* 7.0, $CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 2964, 2935, 1722, 1256, 1215, 1141, 754; EIMS (*m/z*, %): 337 (M^+, 90), 320 (27), 222 (65), 138 (79), 122 (100), 108 (44), 95 (69), 82 (100), 52 (72); HREIMS *m/z* 337.1881 (calcd for $C_{20}H_{29}NO_6$ 337.1881), ^{1}H, ^{13}C NMR and HMBC spectrum see Table 1.

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REFERENCES

1. A. M. Tan, H. P. He, and Z. Mian, *Helv. Chim. Acta*, 2007, **90**, 101.
2. A. M. Tan, Y. S. Li, H. Yang, Z. T. Wang, H. P. He, M. Zhang, and X. J. Hao, *Chinese Chemical Letter*, 2004, **15**, 68.
3. C. G. Logie, M. R. Grue, and J. R. Liddell, *Phytochemistry*, 1994, **37**, 43.
4. A. R. Mattocks, 'Chemistry and Toxicology of Pyrrolizidine Alkaloids', Academic Press, London, 1986, p. 117.