Chemistry of Natural Compounds, Vol. 48, No. 4, September, 2012 [Russian original No. 4, July–August, 2012]

A NEW LIGNAN FROM THE ROOTS OF *Stellera chamaejasme*[a]

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UDC 547.972

*A new lignan, stellerachama A (**1**), was isolated from the roots of* Stellera chamaejasme. *The structure of the new compound was elucidated by analysis of spectrometric data.*

Keywords: lignan, *Stellera chamaejasme*, cytotoxicity.

Stellera chamaejasme (Thymelaeaceae) is a toxic perennial herb widespread in northern and southwestern China. Its roots, known as Langdu, have been used in traditional Chinese medicine (TCM) as herbal remedy for scabies, tinea, and tuberculosis. Previous studies on the chemical constituents of the roots of this plant have shown the presence of diterpenoids [1–3], biflavonoids [4–6], and lignans [7]. In the course of screening for biologically and chemically novel anticancer agents from Chinese herbs, *Stellera chamaejasme* was chosen for phytochemical investigation. In this article, we describe the isolation and structural elucidation of a new lignan compound, stellerachama A (**1**), and its cytotoxic activity.

Stellerachama A (**1**), a colorless gum, exhibited the molecular formula $C_{30}H_{30}O_8$ by HR-EI-MS at *m/z* 518.1921. The UV spectrum had absorption at 282 nm. The ^{1}H NMR spectrum (Table 1) showed signals for three methoxyl group protons at δ 3.81 (3H, s), 3.80 (3H, s), and 3.90 (3H, s), two oxygenated methylene at δ 3.88, 4.14 (2H, m), and 4.24 (2H, m), one oxygenated methine at δ 4.75 (1H, d, J = 4.0), and eight aromatic protons, including two sets of the ABX spin system at δ 6.59 (1H, dd, J = 8.0, 1.5), 6.61 (1 H, d, J = 1.5), and 6.80 (1H, d, J = 8.0), 6.82 (1H, dd, J = 8.2, 1.5), 6.88 (1H, d, J = 8.2), and 6.89 (1H, d, J = 1.5) and one set of the AB spin system at δ 6.41 (1H, d, J = 8.0) and 6.50 (1H, d, J = 8.0). The ^{13}C NMR spectrum (Table 1) revealed the signals for three oxygenated methyl, four methylene (two oxygenated), twelve methine (eight aromatic, one oxygenated), and eleven quaternary (ten aromatic, one carbonyl) carbons. From the above observations, **1** was suggested to be a lignan skeleton compound. Further studies on its ^{1}H and ^{13}C NMR spectral data revealed that these data of **1** were very similar to those of lappaol A, a lignan from *Arctium fructus* [8]. The main difference was that the chemical shift of C-9″ at δ 64.0 in lappaol A was shifted to δ 71.7 in **1**, suggesting that C-9″ of **1** is located in the ring system instead of in the free methylene in lappaol A. This was supported by HMBC correlations of H-9″ with C-5′ and C-6′ (Fig. 1), and confirmed further by calculation of the degrees of unsaturation of **1**.

Further analysis of the HMBC, HMQC, and ^{1}H–^{1}H COSY spectra confirmed the planar structure of **1**. In the ROESY spectrum, correlations of H-8 with H-8′, and H-7″ with H-8″ were not observed, suggesting that H-8/H-8′ and H-7″/H-8″ were in the *trans*-conformation. The relative stereochemistry was confirmed further by minimize energy model using Chemoffice software. On the basis of the above evidence, the structure of **1** was established, and it was named stellerachama A.

In the primary bioassay, compound **1** was tested against four human cancer cell lines, A549, BEL7402, HCT-116, and MDA-MB-231 and only showed weak cytotoxic activity against tumor cell line MDA-MB-231 with IC_{50} value of 60.6 μg/mL.

[a]Materials presented at the 9th International Symposium on the Chemistry of Natural Compounds (SCNC, People′s Republic of China, Urumqi, Oct. 16–19, 2011).

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0009-3130/12/4804-0559

TABLE 1. ^{1}H NMR and ^{13}C NMR Data for **1** ($CDCl_3$, δ, ppm, J/Hz)

C atom	δ_C	δ_H	C atom	δ_C	δ_H
1	129.5 (s)		7′	38.3 (t)	2.52, 2.60 (m)
2	111.5 (d)	6.61 (d, J = 1.5)	8′	41.0 (d)	2.46 (m)
3	146.7 (s)		9′	71.3 (t)	3.88, 4.14 (m)
4	144.5 (s)		1″	129.7 (s)	
5	114.1 (d)	6.80 (d, J = 8.0)	2″	108.6 (d)	6.89 (d, J = 1.5)
6	122.1 (d)	6.59 (dd, J = 8.0, 1.5)	3″	146.6 (s)	
7	34.6 (t)	2.88, 2.93 (m)	4″	146.7 (s)	
8	46.6 (d)	2.55 (m)	5″	114.3 (s)	6.88 (d, J = 8.2)
9	178.8 (s)		6″	118.9 (d)	6.82 (dd, J = 8.2, 1.5)
1′	129.8 (s)		7″	85.9 (d)	4.75 (d, J = 4.0)
2′	110.9 (d)	6.41 (d, J = 8.0)	8″	54.2 (d)	3.09 (m)
3′	121.3 (d)	6.50 (d, J = 8.0)	9″	71.7 (t)	4.24 (m)
4′	144.4 (s)		3-OMe	55.9 (q)	3.90 (s)
5′	132.9 (s)		3″-OMe	55.8 (q)	3.81 (s)
6′	145.3 (s)		4″-OMe	55.8 (q)	3.80 (s)

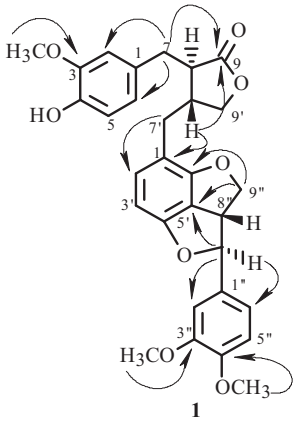

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Fig. 1. The key HMBC correlations of compound **1**.

EXPERIMENTAL

General Methods. UV spectra were recorded by a Shimadzu UV-2550 UV-visible spectrophotometer. IR spectra were recorded using a Nicolet Magna FT-IR spectrophotometer. NMR spectra were run in $CDCl_3$ on a Varian Mercury NMR spectrometer at 400 MHz for ^{1}H and 100 MHz for ^{13}C. EI and HR-EI-MS were measured using a Finnigan/MAT 95 mass spectrometer. Column chromatographic separations were carried out on silica gel H-60 (Qingdao Marine Chemical Group Corporation, Qingdao, China) and Sephadex LH-20 (Pharmacia Biotech AB, Uppsala, Sweden). HSGF254 silica gel TLC plates (Yantai Chemical Industrial Institute, Yantai, China) were used for analytical TLC. All solvents used were of chemical grade (Shanghai Chemical Co. Ltd, Shanghai, China).

Plant Material. *Stellera chamaejasme* was collected in Qinhai Province of China in October, 2009 and were identified by Dr. Z. B. Guan from the Yunnan Branch of the Institute of Medicinal Plants, Chinese Academy of Medical Sciences. Voucher specimens are kept in the "Herbarium" of the Institute.

Extraction and Isolation. The air-dried and powdered roots of *Stellera chamaejasme* (5.0 kg) were extracted exhaustively with 95% EtOH at room temperature. The extract was concentrated in vacuo to yield an EtOH extract, which was then suspended in distilled water and partitioned successively with petroleum ether, $CHCl_3$, EtOAc, and *n*-BuOH. The obtained $CHCl_3$ extract (300 g) was applied to a silica gel column and eluted with a gradient petroleum ether–EtOAc solvent system of increasing polarity (10:1–1:1) to afford five fractions (A–E). Fraction B was subjected to repeated column chromatography over silica gel (petroleum ether–EtOAc, 5:1; 2:1) and Sephadex LH-20 eluted with $CDCl_3$–MeOH (1:1) to afford compound **1** (12 mg).

Stellerachama A (1). Colorless gum. UV spectrum (CH_3OH, λ_{max}, nm) (log ε): 282 (4.10), 230 (4.53). For ^1H NMR and ^{13}C NMR spectral data, see Table 1.

ACKNOWLEDGMENT

Financial support from the National Natural Science Foundation (Grant Nos. 81001369 and 31170327) and the Fundamental Research Funds for the Central Universities (No. 2000219078) of the People′s Republic of China is gratefully acknowledged.

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