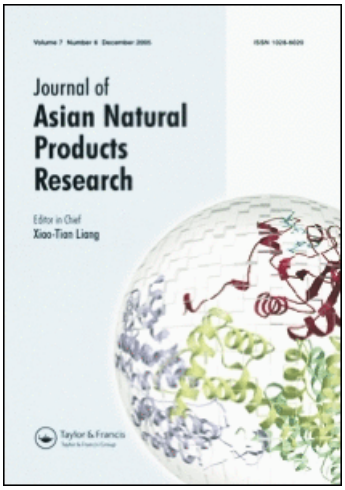

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

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To cite this Article Wang, Li , Zhao, Jing-Feng , Zeng, Xiang-Hui , Xie, Ming-Jin , Yang, Xiao-Dong , Zhang, Hong-Bin and Li, Liang(2009) 'A novel aryltetralone lignan from *Litsea pedunculata*', Journal of Asian Natural Products Research, 11: 12, 1028 — 1031
To link to this Article: DOI: 10.1080/10286020903357525
URL: http://dx.doi.org/10.1080/10286020903357525

Journal of Asian Natural Products Research
Vol. 11, No. 12, December 2009, 1028–1031

A novel aryltetralone lignan from *Litsea pedunculata*

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(*Received 28 June 2009; final version received 21 September 2009*)

A novel aryltetralone lignan, pedunculine A (**1**), together with a known lignan cagayanone A (**2**), was isolated from the leaves and twigs of *Litsea pedunculata*. The structure of the new lignan was elucidated on the basis of spectroscopic methods and single-crystal X-ray diffraction.

Keywords: *Litsea pedunculata*; Lauraceae; aryltetralone lignan; pedunculine A

1. Introduction

The genus *Litsea* (Lauraceae) has about 72 species, and is distributed in South and Southwest China [1]. Most *Litsea* plants contain alkaloids [2–4], flavonoids [5,6], terpenes [7,8], lactones [9], and volatile oil constituents [10]. *Litsea* plants exhibit a variety of biological activities, including antimicrobial, hypothermic, and antitumor effects [2,11,12]. Although *Litsea pedunculata* has been used in traditional Chinese medicine for a long time, no phytochemical investigation has been carried out previously. As a part of our systematic studies on the chemical constituents of medicinal plants of *Litsea* species growing on the Yunnan–Tibet plateau [13–16], we initiated a chemical study on *L. pedunculata*. A new aryltetralone lignan, pedunculine A (**1**), and a known lignan, cagayanone A (**2**) [17], have been isolated from the title plant (Figure 1). To the best of our knowledge, this is the first report on the presence of aryltetralone lignan in the plants of the genus *Litsea*. In this paper, we report on the isolation and structural elucidation of the new lignan from this plant.

2. Results and discussion

Pedunculine A (**1**) was isolated as colorless crystals. Its molecular formula was determined as $C_{20}H_{18}O_6$ by HR-ESI-MS at *m/z* 377.1010 $[M+Na]^+$. The IR spectrum of **1** showed characteristic absorption bands of a hydroxyl group at 3486 cm^{-1}, an aromatic ketone at 1664 cm^{-1}, and an aromatic ring at 1609 and 1504 cm^{-1}. The UV absorption maxima at 295 (3.5) and 317 (3.8) nm also confirmed the existence of these unsaturated functional groups.

The ^1H NMR spectrum (Table 1) displayed aromatic ring signals of ABX-type at δ_H 6.25 (d, $J = 1.9$ Hz, H-2′), 6.65 (dd, $J = 7.8$, 1.9 Hz, H-6′), and 6.78 (d, $J = 7.8$ Hz, H-5′), and other aromatic ring signals at δ_H 6.50 (s, H-3) and 7.42 (s, H-6); two $-OCH_2O-$ at δ_H 5.96 and 5.97; two methine protons at δ_H 2.29 and 3.62; two methyl protons at δ_H 1.27 and 0.98;

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ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020903357525
http://www.informaworld.com

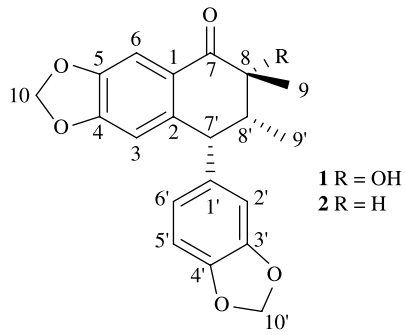

Figure 1. The structures of compounds **1** and **2**.

and an OH group at δ_H 4.05. The ^{13}C NMR spectrum displayed 20 carbons, including 12 aromatic carbons assigned to the two phenyl rings at δ_C 124.2, 143.6, 108.9, 152.8, 147.2, and 105.9 and δ_C 136.8, 109.2, 148.2, 146.7, 108.1, and 123.0; one ketone at δ_C 200.7; two methylenedioxy carbons at δ_C 101.8 and 101.1; two methyls at δ_C 19.1 and 12.2; and three remaining sp^3-hybridized carbons at δ_C 51.4, 46.4, and 75.5. These spectral data indicated that the structure of **1** was rather similar to that of cagayanone A (**2**), except that a hydroxyl group at C-8 (δ 75.5) in **1** replaced the C-8 (δ 42.8) hydrogen in **2**. The ESI-MS of **1**, exhibiting a molecular ion at *m/z* 355 $[M+H]^+$, 16 daltons larger than compound **2**, also confirmed the above results.

In the $^1H-^1H$ COSY spectrum (Figure 2), the correlation of H-7′/H-8′ suggested that the hydroxyl group was located at C-8. The relative configuration of **1** was determined by the NOESY experiment (Figure 2). The NOESY correlations of H-9/H-7′ and H-9/H-8′ indicated β-orientation of these protons. Thus, the aromatic ring at C-7′, OH-8, and Me-9′ was oriented on the opposite side. The relative configuration of **1** was further confirmed by the single-crystal X-ray diffraction, as shown in Figure 3. Therefore,

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

	1		**2**	
No.	^1H (*J*, Hz)	δ_C	^1H (*J*, Hz)	δ_C
1	–	124.2s	–	127.0s
2	–	143.6s	–	140.9s
3	6.50 (s)	108.9d	6.48 (s)	108.9d
4	–	152.8s	–	152.3s
5	–	147.2s	–	147.2s
6	7.42 (s)	105.9d	7.46 (s)	105.8d
7	–	200.7s	–	199.4s
8	–	75.5s	2.77 (m)	42.8d
9	1.27 (s)	19.1q	0.93 (d, $J = 7.0$)	11.8q
10	5.96 (s)	101.8t	5.94 (s)	101.7t
1′	–	136.8s	–	137.4s
2′	6.25 (d, $J = 1.9$)	109.2d	6.38 (d, $J = 1.8$)	109.5d
3′	–	148.2s	–	147.9s
4′	–	146.7s	–	146.3s
5′	6.78 (d, $J = 7.8$)	108.1d	6.70 (d, $J = 8.4$)	108.1d
6′	6.65 (dd, $J = 7.8, 1.9$)	123.0d	6.50 (dd, $J = 8.4, 1.8$)	122.1d
7′	3.62 (d, $J = 11.1$)	51.4d	3.88 (d, $J = 5.8$)	50.6d
8′	2.29 (m)	46.4d	2.36 (m)	42.1d
9′	0.98 (d, $J = 6.3$)	12.2q	1.08 (d, $J = 7.0$)	15.9q
10′	5.97 (s)	101.1t	5.90 (s)	101.1t
8-OH	4.05 (s)			

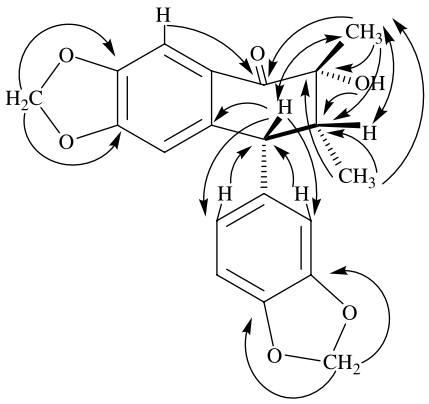

Figure 2. Key $^1H-^1H$ COSY (–), HMBC (→), and NOESY (↔) correlations of **1**.

the structure of **1** was identified as (7′*R*,8*S*,8′*R*)-8-hydroxy-3′,4′,4,5-bis(methylenedioxy)-2,7′-cyclolignan-7-one (pedunculine A, **1**).

The cytotoxicities of compounds **1** and **2** *in vitro* against HL60 (myeloid leukemia), A431 (epidermoid carcinoma), and HepG2 (liver carcinoma) human tumor cell lines were evaluated, and compound **1** exhibited moderate cytotoxic activities against HL60 and A431 cell lines (Table 2).

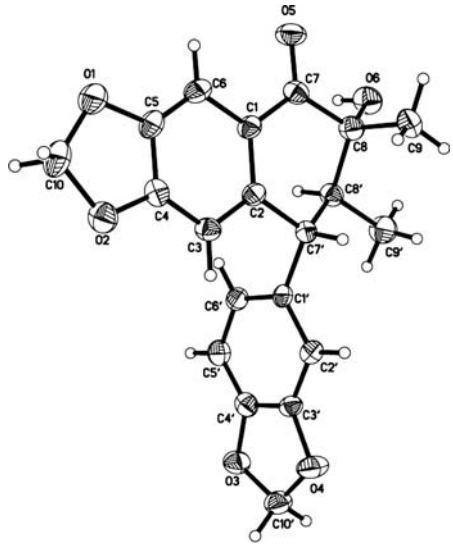

Figure 3. X-ray single-crystal structure of **1**.

3. Experimental

3.1 General experimental procedures

Melting points were recorded on an XT-4 melting point apparatus and are uncorrected. Optical rotations were measured on a Jasco-20 C digital polarimeter. UV spectra were determined on a UV 210A spectrometer and IR spectra on a Bio-Red FTS-135 spectrometer. Both 1D and 2D NMR spectra were determined on a DRX-500 instrument with TMS as the internal reference. ESI-MS was recorded on a VG Auto spec-3000 mass spectrometer. HR-ESI-MS was carried out on an API Qstar Pulsar spectrometer. Commercial Sigel plates (Qingdao Haiyang Chemical Group Co., Qingdao, China) were used for TLC.

3.2 Plant material

The plant material was collected in Luchun Country, Yunnan Province, China, in September 2008, and identified as *L. pedunculata* by Prof. Zhi-Hao Hu (Yunan University). A voucher specimen (No. 07-005) is deposited in the Key Laboratory of Medicinal Chemistry for Natural Resources, Yunnan University, Kunming, China.

3.3 Extraction and isolation

The leaves and twigs of *L. pedunculata* (16.5 kg) were extracted four times with 95% EtOH (4 × 20 liters) at room temperature for 9 days, and the combined extracts were concentrated *in vacuo*. The residue (1.1 kg) was suspended in H_2O and then partitioned with petroleum ether (4 × 1.5 liters), CH_2Cl_2 (4 × 1.5 liters), and EtOAc (6 × 1.5 liters), successively. The petroleum ether extract (153.46 g) was subjected to column chromatography over silica gel (1.8 kg, 100–200 mesh), eluting with petroleum ether–EtOAc (10:1, 8:2, 6:4, 1:1, 4:6, 2:8, and 1:10), to afford 11 fractions (A–K). Fraction G (1.67 g) was purified by column chromatography and

Table 2. Cytotoxic activities data for compounds **1** and **2** [IC_{50} (μg/ml)].

Cells	HL60	A431	HepG-2
1	43.5	60.3	165
2	570.9	322.4	709

eluted with petroleum ether–EtOAc (1:0–0:1) to yield compounds **1** (10 mg) and **2** (15 mg).

3.3.1 Compound (*1*)

(7′*R*,8*S*,8′*R*)-8-Hydroxy-3′,4′,4,5-bis(methylenedioxy)-2,7′-cyclolignan-7-one (pedunculine A); $C_{20}H_{18}O_6$; colorless crystals; mp 168–170°C; $[\alpha]_D^{25} = -111.2$ ($c = 0.222$, $CHCl_3$); UV (MeOH) λ_{max} (log ε): 295 (3.5), 317 (3.8) nm; IR (film) ν_{max}: 3486, 3021, 2962, 2915, 2866, 1855, 1745, 1664, 1609, 1504, 1484, 1445, 1383, 1279, 1234, 1093, 1037, 932, 883, 820, 764 cm^{-1}; ^1H and ^{13}C NMR spectra, see Table 1; ESI-MS: *m/z* 355 $[M+1]^+$(1), 340 (100), 337 (4), 307 (3), 285 (2), 211 (10), 155 (3), 149 (2); HR-ESI-MS: *m/z* 377.1010 $[M+Na]^+$ (calcd for $C_{20}H_{18}NaO_6$, 377.1001). Crystallographic data for **1**: $C_{20}H_{18}O_6$, $M = 354.34$, monoclinic, space group *C*2, $a = 20.464$ (5) Å, $b = 7.0021$ (16) Å, $c = 13.888$ (3) Å, $V = 1642.5(7)$ $Å^3$, $Z = 4$, $d = 1.433$ mg/m^3. Crystal size $0.20 \times 0.13 \times 0.04$ mm, measured on a Bruker apex II diffractometer with a graphite monochromator (ω = scans $2\theta_{max} = 56.6°$), Mo Kα radiation. The total number of independent reflections measured was 5362, of which 2802 were observed ($|F|^2 \geq 3\sigma|F|^2$). Final indices: $R_F = 0.0600$, $R_W = 0.1113$ ($W = 1/\sigma|F|^2$). The crystal structure of **1** was determined by direct methods using SHELXS-97 and expanded using difference Fourier techniques, refined by the SHELXL-97 program and full-matrix least-squares calculations.

Acknowledgements

This work was financially supported by the National Natural Science Foundation of China (30960460), the Natural Science Foundation of Yunnan Province (2007B0006Z), and Training Program Foundation for Key Teacher of Yunnan University, which are gratefully acknowledged.

References

[1] X.H. Yan, F.X. Zhang, H.H. Xie, and X.Y. Wei, *J. Trop. Subtrop. Bot.* **2**, 171 (2000).
[2] D.S. Bhakuni and S. Gupta, *Planta Med.* **48**, 52 (1983).
[3] S. Tewari, D.S. Bhakuni, and M. Dhar, *Phytochemistry* **11**, 1149 (1972).
[4] R.C. Rastogi and N. Borthakur, *Phytochemistry* **19**, 998 (1980).
[5] H.S. Mohan and H.D. Pathak, *Nat. Appl. Sci. Bull.* **27**, 95 (1975).
[6] J.A. Lopez, W. Barillas, and G.L. Jorge, *Planta Med.* **61**, 198 (1995).
[7] E.H. Hakim, S.A. Achmad, M. Effendy, E.L. Ghisalberti, D.C.R. Hockless, and A.H. White, *Aust. J. Chem.* **46**, 1355 (1993).
[8] S.A. Achmad, E.L. Ghisalberti, E.H. Hakim, L. Makmur, and M. Mamurung, *Phytochemistry* **31**, 2153 (1992).
[9] H. Tanaka, T. Nakamura, K. Ichino, K. Ito, and T. Tanaka, *Phytochemistry* **29**, 857 (1990).
[10] K.P. Padmakumari and C.S. Narayannan, *J. Essent. Oil Res.* **4**, 87 (1992).
[11] L.Q.N. Huang, M.L. Shu, and P.R. Chen, *Nat. Prod. Dev. Res.* **6**, 1 (1994).
[12] N.K. Hart, S.R. Johns, J.A. Lamberton, J.W. Loder, A. Moorhouse, A.A. Sioumis, and T.K. Smith, *Aust. J. Chem.* **22**, 2259 (1969).
[13] J.H. Yang, L. Li, Y.S. Wang, J.F. Zhao, H.B. Zhang, and S.D. Luo, *Helv. Chim. Acta* **88**, 2532 (2005).
[14] Y. Xiao, J.F. Zhao, X.D. Yang, G.P. Li, H.B. Zhang, and L. Li, *J. Asian Nat. Prod. Res.* **8**, 411 (2006).
[15] Y. Xiao, J.F. Zhao, X.D. Yang, R. Huang, and L. Li, *Acta Bot. Yunnan.* **27**, 695 (2005).
[16] Y. Xiao, H.J. Zhou, X.D. Yang, J.F. Zhao, and L. Li, *Chin. Tradit. Herb. Drugs* **36**, 1142 (2005).
[17] T.D. Silva and L.M.X. Lopes, *Phytochemistry* **67**, 929 (2006).