Natural Product Research: Formerly Natural Product Letters

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gnpl20

A new Pinoresinol-type lignan from Ligularia Kanaitizensis

Yun-Sen Li [a], Zheng-Tao Wang [b], Main Zhang [b], Shi-De Luo [c] & Ji-Jun Chen [c]

[a] Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 201203, P.R. China

[b] Department of Pharmacognosy, China Pharmaceutical University, Nangjing, 210038, P.R. China

[c] Laboratory of Phytochemistry, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, 650204, P.R. China

Version of record first published: 17 Aug 2006

To cite this article: Yun-Sen Li, Zheng-Tao Wang, Main Zhang, Shi-De Luo & Ji-Jun Chen (2005): A new Pinoresinol-type lignan from Ligularia Kanaitizensis , Natural Product Research: Formerly Natural Product Letters, 19:2, 125-129

To link to this article: http://dx.doi.org/10.1080/14786410410001704723

Natural Product Research, Vol. 19, No. 2, February 2005, pp. 125–129

A NEW PINORESINOL-TYPE LIGNAN FROM *LIGULARIA KANAITIZENSIS*

YUN-SEN LI[a,*], ZHENG-TAO WANG[b], MAIN ZHANG[b], SHI-DE LUO[c] and JI-JUN CHEN[c]

[a]*Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 201203, P.R. China;* [b]*Department of Pharmacognosy, China Pharmaceutical University, Nangjing, 210038, P.R. China;* [c]*Laboratory of Phytochemistry, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, 650204, P.R. China*

(Received 12 July 2003; In final form 07 February 2004)

A new pinoresinol-type Lignan, 9α-angloyloxypinoresinol (**1**), was isolated from the roots and rhizomes of *Ligularia kanaitizensis* (Franch.) Hand.-Mazz, in addition to a known compound, 9α-hydroxypinoresinol (**2**). The structure of this new lignan (**1**) was established on the basis of 1D and 2D NMR experiments. Anti-HIV-1 RT biological assay showed that **1** was inhibitory to HIV-1 RT.

Keywords: 9α-Angloyloxypinoresinol; Lignan; *Ligularia kanaitizensis*; Anti-HIV-1 RT activity

INTRODUCTION

The genus *Ligularia* belongs to the tribe Senecioneae, family Compositae, and comprises more than 110 species native to China. Approximately 40 species have been used as traditional Chinese herbs. *Ligularia kanaitizensis* (Franch.) Hand.-Mazz is distributed in Southwest China. Its roots and rhizomes are used for the treatment of coughs and inflammation by local inhabitants [1]. Previous literature reported the presence of eremophilane-type sesquiterenes and pyrolizidine alkaloids in this genus [2,3]. In our course of finding bioactive components from the *Ligularia* genus [4], recently two pinoresinol-type lignans, rarely occurring in this genus, were obtained from the EtOH extract of the roots and rhizomes of *L. kanaitizensis* (Franch.) Hand.-Mazz for the first time. In the present article, we report the isolation and structural elucidation of the new compound 9α-angloyloxypinoresinol (**1**) by analyzing its NMR data. Moreover, biological assay showed that **1** was inhibitory to HIV-1 RT.

*Corresponding author. E-mail: sinodlsia@yahoo.com

Natural Product Research
ISSN 1478-6419 print: ISSN 1029-2349 online © 2005 Taylor & Francis Ltd
http://www.tandf.co.uk/journals
DOI: 10.1080/14786410410001704723

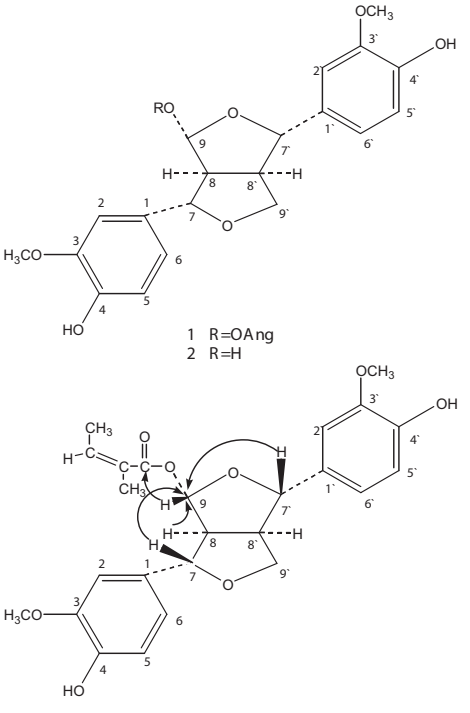

FIGURE 1 The significant HMBC correlation of **1**.

RESULTS AND DISCUSSION

The known compound was determined as 9α-hydroxypinoresinol (**2**) since its physical properties and spectral data were consistent with those in the previous papers [5,6].

Compound **1** was obtained as a colorless gum $[\alpha]_D^{25} = +26.32^\circ$ (*c* 0.42, $CHCl_3$). It had a molecular formula $C_{25}H_{28}O_8$ based on HR-EIMS at *m*/*z* 456.1780 $[M]^+$ (calcd. 456.1784 for $C_{25}H_{28}O_8$) and the ^{13}C NMR data. Its IR spectrum showed the presence of hydroxyl (3419 cm^{-1}) and ester carbonyl groups (1705 cm^{-1}). The ^1H and ^{13}C NMR (DEPT) spectra displayed signals for an angeloyloxyl group (see superscripts b and c in Table I), which was further supported by ion fragment peak at *m*/*z* 356 $[M - AngOH]^+$ in the EIMS spectrum.

Its ^{13}C NMR and DEPT spectra disclosed 25 carbon signals including one carbonyl carbon (δ 166.5), 14 sp^2 carbons, three-oxygenated methine carbon (δ 83.1, 88.6 and 101.4), two methine carbons (δ 52.2 and 61.1), one-oxygenated methylene carbon (δ 72.4), and two-oxygenated methyl carbons (δ 55.9 and 55.7). Except the five carbon signals for the additional angeloyloxyl moiety, the remaining 20 carbon signals of **1** were nearly superimposed on those of **2**, indicating **1** was an angeloyloxyl derivative of 9α-hydroxypinoresinol (**2**). Furthermore, strong HMBC correlations observed between H-9 (δ 6.64 br s) and the carbonyl carbon (δ 166.5) showed the angeloyloxyl moiety connecting with C-9. The relative configuration of H-9 was assigned as β-orientation due to strong correlations between H-7β (δ 5.09 d) and H-9 and H-7′β (δ 5.27 d), and H-9 in the NOESY spectrum. Therefore, the

TABLE I ^{1}H NMR and ^{13}C NMR data of **1** (Solvents: CD_3Cl) and **2** (Solvents: C_5D_5N)

Proton(s) no.	*Compound 1* δ_H *mult. J(Hz)*	*Compound 2* δ_H *mult. J(Hz)*	*Carbon no.*	*Compound 1 DEPT*	*Compound 2 DEPT*
			1	133.0 s	134.1 s
			1′	133.5 s	134.4 s
2	7.05 br s	7.30 d (2.0)	2	108.4 d	110.9 d
2′	7.11 br s	7.64 d (2.0)	2′	108.8 d	111.5 d
			3	145.2 s	147.7 s
			3′	145.2 s	147.9 s
			4	146.6 s	148.7 s
			4′	146.8 s	148.9 s
5	7.00 d (8.9)	7.27 d (8.0)	5	114.2 d	116.3 d
5′	7.02 d (8.5)	7.28 d (8.0)	5′	114.4 d	116.6 d
6	6.97 dd (8.9,1.3)	7.16 dd (8.0,2.0)	6	118.2 d	119.6 d
6′	7.09 dd (8.5,1.2)	7.31 dd (8.0,2.0)	6′	118.6 d	120.0 d
7	5.09 d (6.0)	5.29 d (6.1)	7	83.1 d	84.3 d
7′	5.27 d (6.0)	5.29 d (6.1)	7′	88.6 d	87.9 d
8	3.40 m	3.46 m	8	61.1 d	63.3 d
8′	3.20 m	3.45 m	8′	52.2 d	54.8 d
9	6.64 br s	6.16 d (1.1)	9	101.4 d	102.7 d
9′α	4.49 dd (9.0,5.8)	4.40 dd (9.0,6.1)	9′	72.4 t	72.5 t
9′β	4.22 dd (9.0,2.6)	4.27 dd (9.0,2.0)			
OMe(2)	3.98 q	3.86 q	OMe (2)	55.9 q	56.0 q
	3.96 q	3.85 q		55.7 q	56.0 q
OAng	[b]		OAng	[c]	

[a] chemical shifts (ppm), multiplicity, and coupling constant (Hz in parentheses); [b] $\delta = 6.20$ (1H, qd, $J = 7.2$, 1.4Hz, MeCH=), 2.05 (3H, d, $J = 7.2$Hz, MeCH=), 1.92 (3H, s, MeCCOO); [c] $\delta = 20.1$ (q, *Me*CH=), 139.3 (d, Me*CH*=), 15.5 (q, *Me*CCOO), 127.2 (s, Me*C*COO), 166.5 (s, *C*OO).

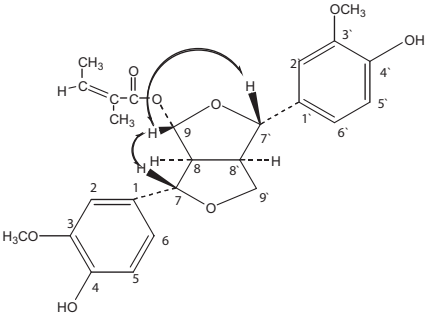

FIGURE 2 The significant NOESY correlation of **1**.

structure of **1** was unambiguously established to be 9α-angloyloxypinoresinol (Figs. 1 and 2).

The two compounds **1** and **2** were subjected to anti-HIV RT biological assay. Compound **1** showed moderate inhibition to HIV RT (inhibition 53.3% at 200 μg/mL). However, compound **2** was inactive against HIV-1 RT.

EXPERIMENTAL

General

Column chromatography (CC): silica gel, 200–300 mesh. TLC: Precoated silica gel GF_{254} plates: detection at 254 UV nm, and by ceric sulfate reagent. Optical rotations: JASCO DEP-370 polarimeter. NMR spectra were recorded on a Bruker AM-400 or DRX-500 instrument with TMS as an internal standard and C_5D_5N as solvents. ^{1}H NMR and ^{1}H-^{1}H COSY spectra were measured at 400.13 or 500.13 MHz; ^{13}C NMR and DEPT spectra were recorded at 100.6 MHz; HMBC spectrum was obtained at 500.13/125.8 MHz. ^{13}C NMR assignments were determined by HMQC and HMBC spectra. EIMS and HR-EIMS data were obtained with a MAT-95 mass spectrometer.

Plant Material

The roots and rhizomes of *L. kanaitizensis* (Franch.) Hand.-Mazz were collected from Yulong Mountain, Lijiang Prefecture of Yunnan Province and authenticated by Dr. Main Zhang. A voucher specimen (No. 990007-Li) is deposited in the Herbarium of China Pharmaceutical University.

Isolation of Constituents

Dried and powdered roots and rhizomes of *Ligularia vellerea* (5.5 kg) were extracted with EtOH (10 L × 3) at room temperature. After removal of solvent *in vacuo*, an extract of 330.0 g was afforded. The extract was suspended in H_2O and partitioned with petroleum ether (60–90°C), EtOAc and *n*-BuOH, successively. Eighty grams of the evaporated EtOAc fraction were subjected to chromatography on a silica gel column (200–300 mesh, 1.0 kg), eluted with $CHCl_3$–Me_2CO mixtures of increasing polarity (30 : 1, 20 : 1, 10 : 1, 5 : 1, and 3 : 1). Six crude fractions were obtained after combining the eluates by TLC monitoring. The third fraction (2 g) was isolated on CC (silica gel 200–300 mesh, 200 g), eluted with $CHCl_3$/$(Me)_2CO$ (10 : 1, 150 mL aliquots), and further purified on a Sephadex LH-20 column (50 g), eluted with $(Me)_2CO$ (5 mL aliquots) to obtain **1** (50 mg) and **2** (40 mg).

9α-hydroxypinoresinol 1

Colorless gum, $[\alpha]_D^{25} = +26.32°$ (*c* 0.42 $CHCl_3$); IR ν_{max}(KBr)cm^{-1}: 3 419 (OH), 2 937, 1 705 (ester C=O), 1 603, 1 517, 1 456, 1 275, 1 159, 1 033, 825, 534; HR-EIMS: 456.1780 $[M]^+$, calcd.: 456.1784 $[M]^+$; EIMS *m*/*z* (%): 456 $[M]^+$ (20), 356 $[M - OAng]^+$ (98), 327 (32), 232 (77), 219 (31), 204 (57), 191 (27), 175 (32), 163 (47), 151 (77), 137 (100), 100 [angelic acid]$^+$ (34), 83 [angeloyloxyl]$^+$ (40), 65 (22); for ^{1}H and ^{13}C NMR data see Table I.

9α-hydroxypinoresinol 2

Colorless gum; EI-MS *m*/*z* (%): 374 $[M]^+$ (96), 356 $[M - H_2O]^+$ (10), 327 (25), 222 (15), 205 (15), 196 (44), 175 (36), 163 (72), 153 (100), 137 (88), 124 (37), 115 (22), 103 (32), 93 (59), 65 (50); for ^{1}H and ^{13}C NMR data see Table I.

Biological Assay

The anti-HIV RT bioassay was accomplished according to the procedures outlined earlier [7]. Positive control: foscarnet. Standards of inhibiting HIV RT: inhibition $\geq$50% at 200 μg/mL.

Acknowledgment

This research was financially supported by the Natural Science Foundation (NSFC) for outstanding young scientists for Wang Z. T. (39825129).

References

[1] Z.Y. Wu (1990). *Xin hua ben cao gan yao*, Vol. III, p. 445. Shanghai science and technology press, Shanghai.
[2] Y. Zhao, Z.J. Jia, H. Peng (1995). *J Nat. Prod.*, **58**, 1358–1364.
[3] Y. Asada, T. Furuya and N. Murakami (1981). *Planta Medica*, **42**, 202–203.
[4] Y.S. Li, S.D. Luo, M. Zhang, J.J. Chen, Z.T. Wang (2001). *Zhongguo Zhongyao Zazhi*, **26**, 835–837.
[5] F. Abe and T. Yamauchi (1988). *Phytochemistry*, **27**, 575.
[6] L. Yang, H. Chen and Z.T. Jia (1995). *Indian J. Chem.*, **34B**, 975.
[7] B.S. Min, H. Miyashiro and M. Hattori (2002). *Phytotherapy Research*, **16**, s57–s62.