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A NEW NORNEOLIGNAN FROM THE LEAVES OF THE TRADITIONAL CHINESE MEDICINE *Artemisia argyi*

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Investigation of the EtOH extract of Artemisia argyi *leaves led to the isolation of six compounds (**1–6**). These structures were identified using spectroscopic methods, of which compound **1**, (+)-artemisarin, is a new norneolignan, and **2–6** were isolated from this plant for the first time.*

Keywords: *Artemisia argyi*, Asteraceae, norneolignan.

Artemisia argyi (Asteraceae) is a common perennial aromatic herb. The leaves of *A. argyi* (Chinese name "Ai-Ye") have been used as a traditional herb for the treatment of bacterial infection and allergy in China [1]. Some formulas that include this herb are also used to treat hemorrhagic diseases such as metrorrhagia and metrostaxis and excreting blood [2]. However, the compounds in the leaves of *A. argyi* are not known so far. Previous reports indicated that the major principles of *A. argyi* are volatile compounds that possess antimicrobial activities [3]. Considering that only a limited number of lignans and low-molecular-weight compounds have been characterized in the leaves of this plant, we initiated this study and isolated six compounds. Among them, compound **1** is a new norneolignan; the others were isolated from this plant for the first time.

Compound **1** was obtained as yellowish oil. The molecular formula $C_{19}H_{18}O_5$ was determinrd from the HR-ESI-MS, ^{13}C NMR, and DEPT spectra. The ^1H NMR spectrum (Table 1) showed two ABX spin systems in the aromatic region. The ^{13}C NMR (Table 1) exhibited 19 carbon signals, which were attributed to two benzene rings, four methylenes (three oxygen bearing ones), and three methines (two olefinic ones). These findinfs indicate that compound **1** is a norneolignan. The ^1H–^1H COSY spectrum showed cross peaks of H-5′/H-6′, H-5″/H-6″, H-4/H-3/H-2/H-5, and H-1/H-2 (Fig. 1), which confirmed the substituted patterns of two benzene rings. The HMBC correlations (Fig. 1) of H-4/C-1″ (δ 131.1), C-2″ (δ 108.8), and C-6″ (δ 122.1), and H-5/C-1′ (δ 132.3), C-2′ (δ 109.5), and C-6′ (δ 122.0) indicated the position of the two benzene rings. H-6/C-3″ (δ 145.8) and C-4″ (δ 147.1) and H-7/C-3′ (δ 146.9) and C-4′ (δ 146.9) indicated the position of methylenedioxy (Fig. 1). The geometry of $\Delta^{3,4}$ was of the *Z*-form, as deduced from the small $J_{H\text{-}3,H\text{-}4}$ value of 11.2 Hz. The absolute configuration at C-2 remains unknown.

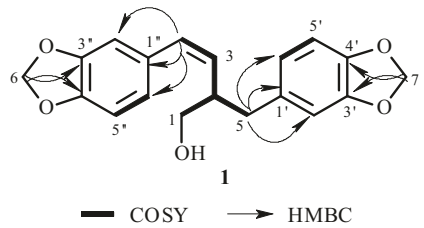

Fig. 1. COSY and HMBC correlations of **1**.

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

C atom	δ_C	δ_H	C atom	δ_C	δ_H
1a	65.8 (CH_2)	3.51 (dd, J = 10.4, 7.6)	3′	146.9 (C)	–
1b		3.62 (dd, J = 10.4, 5.4)	4′	146.9 (C)	–
2	42.4 (CH)	3.13 (m)	5′	108.1 (CH)	6.70 (d, J = 7.9)
3	132.0 (CH)	5.38 (t like, J = 11.2)	6′	122.0 (CH)	6.59 overlap
4	131.9 (CH)	6.51 (d, J = 11.2)	1″	131.1 (C)	–
5a	37.8 (CH_2)	2.55 (dd, J = 13.7, 7.8)	2″	108.8 (CH)	6.59 (d, J = 1.4)
5b		2.69 (dd, J = 13.7, 6.1)	3″	145.8 (C)	–
6	100.8 (CH_2)	5.91 (s)	4″	147.1 (C)	–
7	100.9 (CH_2)	5.93 (s)	5″	108.0 (CH)	6.72 (d, J = 7.8)
1′	132.3 (C)		6″	122.1 (CH)	6.59 overlap
2′	109.5 (CH)	6.61 (d, J = 1.3)			

The known compounds were identified as 7-methoxycoumarin (**2**) [4], demethoxyaschantin (**3**) [5, 6], methyl 4-hydroxyphenylacetate (**4**) [7, 8], umbelliferone (**5**) [9], and scopoletin (**6**) [10] by comparison of their spectroscopic data with literature data or directly from their spectroscopic data.

EXPERIMENTAL

General Experimental Procedures. Optical rotation was recorded on a Horiba SEPA-300 polarimeter. UV spectrum was measured on a Shimadzu UV-2401PC spectrophotometer. IR spectrum was obtained on a Tensor 27 spectrometer with KBr pellet. NMR spectra were recorded on a Bruker AV-400 or DRX-500 spectrometer. ESI-MS were recorded on a VG Auto Spec-3000 spectrometer, and HR-ESI-MS were determined on an API QSTAR Pulsar 1 spectrometer. Column chromatography (CC) was carried out on silica gel (200–300 mesh; Qingdao Marine Chemical Inc., Qingdao, China), RP-18 (40–60 μm; Daiso Co., Osaka, Japan), MCI gel CHP 20P (75–150 μm, Tokyo, Japan), and Sephadex LH-20 (Amersham Pharmacia, Uppsala, Sweden).

Plant Material. The leaves of *A. argyi* were purchased from Yunnan Xianghui Corporation of Materia Medica, Yunnan Province, P. R. China, in November 2011, and authenticated by one of our authors (Y. Q. Li). A voucher specimen (CHYX-0577) was deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, P. R. China.

Extraction and Isolation. The dried powdered leaves of *A. argyi* (50 kg) were extracted with 80% EtOH (7 × 25 L) to give an extract (2500 g), which was suspended in water and partitioned by petroleum ether, EtOAc, and *n*-BuOH (each 3 × 3 L). The EtOAc extract (506 g) was subjected to silica gel CC and eluted with a gradient of $CHCl_3$–MeOH (100:0, 100:1, 96:4, 92:8, 85:15, 0:100) to give fractions A–D. Fraction B (226 g) was subjected to silica gel CC and eluted with a gradient of $CHCl_3$–Me_2CO (100:1, 96:4, 92:8, 90:10, 85:15, 2:1) (B-a–B-e). Fraction B-b (12 g) was submitted to CC over MCI gel CHP 20P eluted with a gradient of aqueous MeOH to yield two subfractions (B-b-1–B-b-2). Fraction B-b-2 (408 mg) was passed through Sephadex LH-20 (MeOH) to yield compound **1** (9.4 mg). Fraction B-b-1 (580 mg) was passed through Sephadex LH-20 (MeOH) to give two subfractions of which one was purified by PTLC (petroleum ether–EtOAc, 6:1) to yield compound **2** (2.5 mg). Fraction B-c (7 g) was separated by RP-18 eluted with a gradient of MeOH–H_2O (20%–100%) followed by Sephadex LH-20 (MeOH) to yield two subfractions (B-c-1 and B-c-2). Fraction B-c-1 (0.8 g) was purified by preparative TLC (petroleum ether–EtOAC, 5:1) followed by semipreparative HPLC (Agilent 1200 liquid chromatograph with a Zorbax SB-C18 column, 9.4 mm × 25 cm, i.d.) eluted with 45% aqueous MeOH to give compound **3** (0.8 mg). Fraction B-c-2 (0.6 g) was purified by preparative TLC (petroleum ether–Me_2CO, 7:1) to afford compound **4** (2.5 mg). Fraction C (47 g) was separated by RP-18 eluted with a gradient of MeOH–H_2O (40%–100%) to yield two subfractions (C-1 and C-2). Fraction C-1 (6.3 g) was separated by Sephadex LH-20 (MeOH) and then purified by preparative TLC (petroleum $CHCl_3$–EtOAc, 12:1) to afford **5** (1.0 mg). Fraction C-2 (0.9 g) was purified by silica gel CC ($CHCl_3$–^{i}PrOH, 60:1) followed by preparative TLC (petroleum ether–Me_2CO, 6:1) to afford **6** (2.5 mg).

(+)-Artemisarin (1). Yellowish oil, $[\alpha]_D^{18}$ –60.7° (*c* 0.27, $CHCl_3$). UV ($CHCl_3$, λ_{max}, nm) (lg ε): 291 (3.02), 266 (3.03), 239.6 (3.04). IR (KBr, ν_{max}, cm^{-1}): 3430, 3006, 2898, 1631, 1611, 1502, 1489, 1442, 1245, 1039. For ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) data, see Table 1. ESI-MS (negative) *m/z* 325 $[M - H]^-$. HR-ESI-MS (negative) *m/z* 326.1153 (calcd for $C_{19}H_{18}O_5$, 326.12).

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