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A new lignan from *Smilax bockii* warb.

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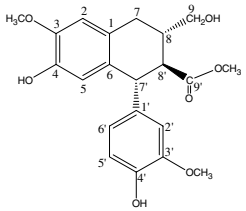
A new lignan named (−)-isolariciresinol 9′-carboxylic acid methyl ester has been isolated from the roots of *Smilax bockii* warb.. The structure of the new lignan was determined on the basis of spectral and chemical studies.

Smilax bockii warb. is a Chinese folk herb and belongs to the family Liliaceae, which is widely distributed in the south of China. It is used to treat rheumatoid arthritis and woman ailments (Guo et al. 2004). In our recent research, we also found its anti-inflammation activity by the method of SEAP (Secreted alkaline phosphatase). The 70% ethanol extract of the roots of *S. bockii* showed moderate activity in inhibiting TNF-α-induced NF-κB in murine macrophage RAW 264.7 cells with an IC_{50} value of 166.6 μg/ml (Xu et al. 2005). We began a study to isolate the effective constituents from the roots of *Smilax bockii* warb. guided by the bioactivity. This paper deals with the structural elucidation of the new compound, (−)-isolariciresinol 9′-carboxylic acid methyl ester.



Compound **1**, white amorphous powder with an $[\alpha]_D^{21}$ value of −46.9° (c = 0.1, MeOH). The molecular formula was determined to be $C_{21}H_{24}O_7$ based on the ion peak at m/z 388 in the EI-MS spectrum together with carbon signals in the ^{13}C NMR spectrum. In addition, the IR spectrum revealed the presence of a hydroxyl group (3363 cm^{-1}), a carbonyl group (1718 cm^{-1}), and an aromatic ring (1513, 1434 cm^{-1}). Its ^1H and ^{13}C NMR spectra showed great similarity to those of (−)-isolariciresinol 4-*O*-β-D-glucopyranoside (Jiang et al. 2001). The ^1H NMR spectrum gave signals due to three methoxyl groups [δ 3.81 (3 H, s), δ 3.75 (3 H, s), δ 3.48 (3 H, s)], δ 6.61 (1 H, d, J = 2.0 Hz), δ 6.71 (1 H, d, J = 8.0 Hz) and δ 6.55 (1 H, dd, J = 8.0, 2.0 Hz) indicated the presence of 1,3,4-trisubstituted benzene ring. Besides the appearance of two singlets at δ 6.66 and δ 6.15 implied a disubstituted benzene ring in the structure. The ^{13}C NMR spectrum provided 21 carbon signals that were assigned to a carbonyl carbon [δ 177.2 (C-9′)], two aromatic nuclei [δ 127.8 (C-1), 112.5 (C-2), 147.7 (C-3), 145.6 (C-4), 116.6 (C-5), 132.3 (C-6) and δ 136.7 (C-1′), 113.5 (C-2′), 149.1 (C-3′), 146.5 (C-4′), 116.0 (C-5′), 123.0 (C-6′)], and five aliphatic carbons [δ 33.2 (C-7), 41.6 (C-8), 65.9 (C-9) and δ 50.5 (C-7′), 54.6 (C-8′)] along with three methoxyl groups [δ 56.4 (3-OCH_3), 56.4 (3′-OCH_3) and 51.9 (9′-OCH_3)]. By analyzing the HMQC, HMBC, and ^1H-^1H COSY NMR spectra, all the proton and carbon signals were assigned unambiguously.

The absolute configuration of C-7′ was established to be R, since a positive Cotton effect at 291 nm was observed in the CD spectrum. Thus compound **1** was determined to be (−)-isolariciresinol 9′-carboxylic acid methyl ester (Jiang et al. 2001).

The anti-inflammation activity of the compound was also tested, yet it showed weak activity in inhibiting the activity of TNF-α-induced NF-κB activation in murine macrophage RAW 264.7 cells.

Experimental

1. Apparatus

Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Melting points were measured on a Yanaco-hot-stage without correction. 1D and 2D NMR spectra were recorded in CD_3OD on a Brucker-ARX-600 spectrometer with TMS as an internal standard. IR spectra were measured on a Perkin-Elmer 2000 FT-2R spectrometer as KBr Pellets. EI-MS were measured on a VG-5050E mass spectrometer. Silica gel (200–300 mesh) for column chromatography and GF_{254} for TLC were produced by Qingdao Ocean Chemical Group Co. of China. Sephadex LH-20 was produced by Merck Co., Germany.

2. Plant material

The roots of *S. bockii* were collected from a county of Hunan province, China, in April 2003. The plant material was identified and a voucher specimen (No. 0030406) was deposited in the Research Department of Natural Medicine, Shenyang Pharmaceutical University, China.

3. Extraction

Dried roots (10 kg) of *S. bockii* were cut into small pieces and extracted three times with 70% ethanol. The ethanol extract (2 kg) was partitioned with $CHCl_3$, EtOAc and *n*-BuOH successively.

4. Isolation and characterization of 1

The EtOAc extract (82 g) was first subjected to column chromatography on silica gel gradiently eluted with $CHCl_3$: MeOH (from 100 : 0 to 100 : 70) to obtain 30 fractions. Fraction 15 was further purified by sephadex LH-20 eluting with $CHCl_3$: MeOH and recrystallization to yield compound **1**.

Compound **1** (10.8 mg): white powder (MeOH); m.p. 109–111 °C; $[\alpha]_D^{21}$ −46.9° (c = 0.1, MeOH). EI-MS: m/z 388 $[M]^+$. CD (c = 0.13 mM, MeOH) [θ] (nm): −7830 (240), −4458 (276), +9527 (291); IR ν_{max} (KBr): 3360, 1719, 1513, 1262, 1123 cm^{-1}. ^1H NMR (600 MHz, CD_3OD): 6.66 (1 H, s, H-2), 6.15 (1 H, s, H-5), 2.91 (1 H, dd, J = 16.5, 4.5 Hz, H-7a), 2.73 (1 H, br. d, J = 16.5 Hz, H-7b), 2.22 (1 H, m, H-8), 3.54 (1 H, dd, J = 11.0, 5.0 Hz, H-9a), 3.48 (1 H, dd, J = 10.5, 5.5 Hz, H-9b), 6.61 (1 H, d, J = 2.0 Hz, H-2′), 6.71 (1 H, d, J = 8.0 Hz, H-5′), 6.55 (1 H, dd, J = 8.0, 2.0 Hz, H-6′), 4.07 (1 H, d, J = 11.0 Hz, H-7′), 2.65 (1 H, t, J = 11.0 Hz, H-8′), 3.81 (3 H, s, 3-OCH_3), 3.75 (3 H, s, 3′-OCH_3), 3.48 (3 H, s, 9′-OCH_3); ^{13}C NMR (125 MHz, CD_3OD): 127.8 (C-1), 112.5 (C-2), 147.7 (C-3), 145.6 (C-4), 116.6 (C-5), 132.3 (C-6), 33.2 (C-7), 41.6 (C-8), 65.9 (C-9), 136.7 (C-1′), 113.5 (C-2′), 149.1 (C-3′), 146.5 (C-4′), 116.0 (C-5′), 123.0 (C-6′), 50.5 (C-7′), 54.6 (C-8′), 177.2 (C-9′), 56.4 (3-OCH_3), 56.4 (3′-OCH_3), 51.9 (9′-OCH_3).

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