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## A new amide alkaloid from the leaves of *Piper sarmentosum*

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A new amide alkaloid, *N*-(3',4',5'-trimethoxy-*cis*-cinnamoyl)pyrrolidine (**1**), named sarmentomicine was isolated from the ethanol extract of the leaves of Malayan *Piper sarmentosum*, together with two known phenylpropanoids. Their structures were elucidated on the basis of spectroscopic analysis.

**Keywords:** *Piper sarmentosum*; Piperaceae; leaves; amide alkaloid

### 1. Introduction

*Piper sarmentosum* Roxb. (Piperaceae) is known as 'daun kadok' in Malaysia. This plant is native to Northeast India, Malaysia, and Indonesia and is now widely grown throughout Southeast Asia and parts of China [1]. In Malaysia and Indonesia, the leaves and roots of this plant are used for the treatment of toothache, coughing, asthma, and pleurisy [2]. In previous investigations of *P. sarmentosum*, several amide alkaloids, phenylpropanoids, and lignans were isolated from the leaves and fruits [3–6]. In this article, we would like to report the isolation and structural elucidation of compounds isolated from the leaves of Malayan *P. sarmentosum*.

### 2. Results and discussion

The ethanol extract of the leaves of Malayan *P. sarmentosum* furnished a new amide alkaloid, *N*-(3',4',5'-trimethoxy-*cis*-cinnamoyl)pyrrolidine (**1**), named sarmentomicine, together with two known phenylpropanoids, asaricin (**2**) [4] and  $\gamma$ -asarone (**3**) [4].

Sarmentomicine (**1**) (Figure 1) was isolated as a colorless oil. The EI-MS of **1** showed a molecular ion at  $m/z$  291 and HR-EI-MS measurements at  $m/z$  291.1475 established the molecular formula as  $C_{16}H_{21}NO_4$ , indicating seven degrees of unsaturation. The UV spectrum showed absorption maxima at 225 and 280 nm. The IR spectrum indicated the presence of the absorption band at  $1636\text{ cm}^{-1}$  (C=O amide). The  $^1\text{H}$  NMR spectrum displayed signals for two aromatic protons at  $\delta$  6.73 (2H, s), three methoxy groups at  $\delta$  3.85 (3H, s) and 3.84 (6H, s), and a pair of AB doublets at  $\delta$  6.02 (1H, d,  $J = 12.4$  Hz) and 6.54 (1H, d,  $J = 12.4$  Hz), indicating the presence of a 3',4',5'-trimethoxycinnamoyl moiety in compound **1**. The coupling constant of 12.4 Hz indicated that the C=C double bond of the 3',4',5'-trimethoxycinnamoyl moiety possessed a *cis* geometry configuration [7]. A similar compound (**4**) also possessed a *cis* cinnamoyl moiety isolated from *Piper nigrum* [7]. The presence of the 3',4',5'-trimethoxycinnamoyl moiety in compound **1** can be further corroborated from the  $^{13}\text{C}$

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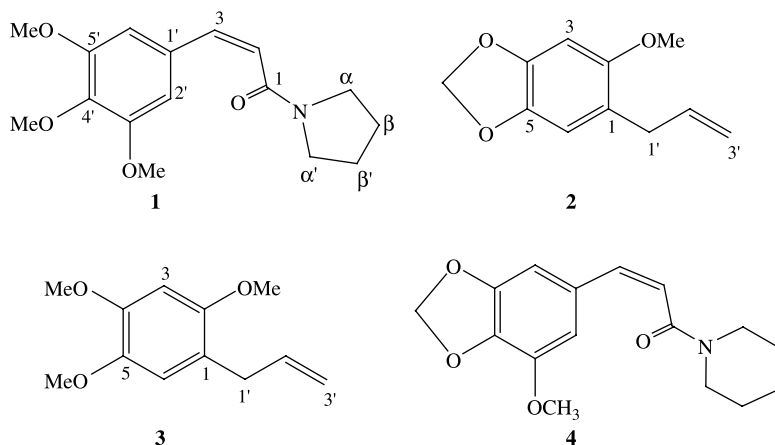


Figure 1. Structures of compounds **1**–**4**.

NMR spectrum, which indicated signals for six aromatic carbons at  $\delta$  105.6 ( $2 \times$ ), 131.3, 141.9, and 153.2 ( $2 \times$ ), two olefinic carbons at  $\delta$  123.8 and 133.3, one carbonyl carbon at  $\delta$  167.3, and three methoxy carbons at  $\delta$  56.2 ( $2 \times$ ) and 61.0. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **1** also showed signals due to a pyrrolidine ring at  $\delta_{\text{H}}$  3.51 (2H, t,  $J = 6.4$  Hz, H- $\alpha$ ), 3.23 (2H, t,  $J = 6.4$  Hz, H- $\alpha'$ ), 1.85 (2H, m, H- $\beta$ ), and 1.81 (2H, m, H- $\beta'$ ) and  $\delta_{\text{C}}$  47.1 (C- $\alpha$ ), 45.5 (C- $\alpha'$ ), 25.9 (C- $\beta$ ), and 24.4 (C- $\beta'$ ), respectively. Due to the higher barrier to rotation about the carbonyl–nitrogen bond, the H- $\alpha'$  and C- $\alpha'$  (*syn* to the carbonyl group) resonate upfield from the H- $\alpha$  and C- $\alpha$  (*anti* to the carbonyl group) [8,9]. From the  $^1\text{H}$ – $^1\text{H}$  2D COSY and HMQC experiments, the H- $\beta$  and C- $\beta$  resonate downfield from the H- $\beta'$  and C- $\beta'$ . In the HMBC spectrum, important long-range correlations were observed between C-1 ( $\delta$  167.3) and H-2 ( $\delta$  6.02), H-3 ( $\delta$  6.54), H- $\alpha'$  ( $\delta$  3.23), and H- $\alpha$  ( $\delta$  3.51); C-3 ( $\delta$  133.3) and H-2 ( $\delta$  6.02), H-2' ( $\delta$  6.73), and H-6' ( $\delta$  6.73); C-1' ( $\delta$  131.3) and H-2 ( $\delta$  6.02), H-3 ( $\delta$  6.54), H-2' ( $\delta$  6.73), and H-6' ( $\delta$  6.73); C- $\alpha'$  ( $\delta$  45.5) and H- $\beta'$  ( $\delta$  1.81) and H- $\beta$  ( $\delta$  1.85); C- $\alpha$  ( $\delta$  47.1), and H- $\beta'$  ( $\delta$  1.81) and H- $\beta$  ( $\delta$  1.85) (Figure 2). Consequently, compound **1** is therefore elucidated as *N*-(3',4',5'-tri-

methoxy-*cis*-cinnamoyl)pyrrolidine, named sarmentomicine.

### 3. Experimental

#### 3.1 General experimental procedures

The UV spectra were obtained on a Perkin-Elmer Lambda 35 UV/vis spectrophotometer, whereas the IR spectra were recorded on a Perkin-Elmer Spectrum RX1 FT-IR spectrophotometer. EI-MS and HR-EI-MS were obtained on a Finnigan MAT95XL-T mass spectrometer.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded in  $\text{CDCl}_3$  (Merck, Darmstadt, Germany) using TMS as the internal standard on a JEOL JNM-LA400 spectrometer at 400 and 100 MHz, respectively. Centrifugal TLC was performed on a chromatotron model 7924T over silica gel Merck 7749. Silica gel Merck 9385 was used for vacuum

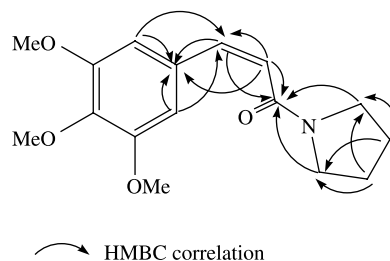


Figure 2. HMBC correlations of **1**.

column chromatography. Silica gel 60F<sub>254</sub> Merck was used for TLC. Spots on TLC plates were visualized by exposure to iodine vapors, UV radiation, and by Dragendorff's reagent. All solvents were distilled prior to use.

### 3.2 Plant material

The leaves of *P. sarmentosum* used in this study were collected in Penang, Malaysia, in May 2006, and identified by Meng-Chew Chuah, Department of Science, Universiti Tunku Abdul Rahman. A voucher specimen (No. M-2006-05) has been deposited at the Herbarium of the Department of Science, Universiti Tunku Abdul Rahman, Malaysia.

### 3.3 Extraction and isolation

The dried leaves (5 kg) were ground and extracted with 95% EtOH (15 L × 3, 7 days each) at room temperature. After filtration and evaporation, the concentrated ethanol extract was partitioned in distilled water (1 L). The mixture was then extracted successively with chloroform (2 L × 3). Evaporation of the chloroform gave a dark green oil (45.7 g). The chloroform crude extract was separated by initial vacuum column chromatography on silica gel with CHCl<sub>3</sub> with increasing proportions of MeOH, followed by rechromatography of appropriated partial fractions by centrifugal TLC. Initial vacuum column chromatography of the chloroform crude extract provided 10 main fractions. Rechromatography of fraction 1 with CHCl<sub>3</sub>, followed by centrifugal TLC (*n*-hexane–diethyl ether 5:1), gave compounds **2** (150 mg) and **3** (100 mg). Compound **1** (12 mg) was isolated from fraction 7 by centrifugal TLC using *n*-hexane–EtOAc (1:4) as the eluent.

#### 3.3.1 Sarmentomicine (**1**)

A colorless oil; UV (EtOH)  $\lambda_{\max}$  (log  $\epsilon$ ): 225 (3.86), 280 (3.45) nm. IR (dry film)

Table 1. <sup>1</sup>H and <sup>13</sup>C NMR spectral data of compound **1** (400 MHz for <sup>1</sup>H, 100 MHz for <sup>13</sup>C, CDCl<sub>3</sub>).

Position	$\delta_C$	$\delta_H$
1	167.3	
2	123.8	6.02 d (12.4)
3	133.3	6.54 d (12.4)
1'	131.3	
2'	105.6	6.73 s
3'	153.2	
4'	141.9	
5'	153.2	
6'	105.6	6.73 s
$\alpha$	47.1	3.51 t (6.4)
$\beta$	25.9	1.85 m
$\alpha'$	45.5	3.23 t (6.4)
$\beta'$	24.4	1.81 m
3'-OCH <sub>3</sub>	56.2	3.84 s
4'-OCH <sub>3</sub>	61.0	3.85 s
5'-OCH <sub>3</sub>	56.2	3.84 s

$\nu_{\max}$ : 2942, 1636, 1606, 1581, 1505, 1417, 1329, 1240, 1125, 1006 cm<sup>-1</sup>. <sup>1</sup>H and <sup>13</sup>C NMR spectral data, see Table 1; EI-MS *m/z* (rel. int.): 291 (M<sup>+</sup>, 71), 222 (90), 221 (100), 206 (11), 190 (26), 179 (21), 163 (14), 147 (10); HR-EI-MS *m/z*: 291.1475 [M]<sup>+</sup> (calcd for C<sub>16</sub>H<sub>21</sub>NO<sub>4</sub>, 291.1471).

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