



# Isopiperolein B: an alkamide from *Piper nigrum*<sup>☆</sup>

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## Abstract

A new pyrrolidine alkamide, Isopiperolein B has been isolated from the berries of *Piper nigrum*. Its structure was established as 1-[(*E*)-10-(3,4-methylenedioxyphenyl)-dec-9-enoyl]pyrrolidine based on degradative and spectroscopic evidence. © 1999 Elsevier Science Ltd. All rights reserved.

**Keywords:** *Piper nigrum*; Piperaceae; Black Pepper; Isopiperolein B

## 1. Introduction

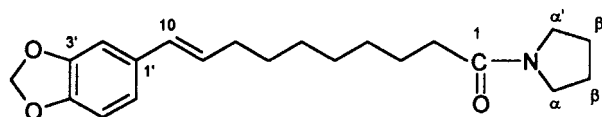
*Piper nigrum* L. (black pepper) finds extensive use in the Ayurvedic system of medicine (Kirtikar & Basu, 1981). A number of piperidine and pyrrolidine alkaloids are known to occur in *Piper nigrum* (Parmar et al., 1997; Sumathy Kutty, 1993), the most important being piperine, known to possess a variety of biological properties e.g. CNS stimulant, analgesic, antipyretic and antifeedant activities (Miyakado, Nakayama, Yoshioka & Nakatani, 1979). Traditionally the aqueous extract of black pepper is used in Ayurvedic preparations, but as part of our programme on the chemistry of the aqueous extract, we have reinvestigated the petrol (used for defatting) extract from which a new pyrrolidine alkamide, isopiperolein B has been isolated.

## 2. Results and discussion

The petrol extract of the berries of *Piper nigrum* on repeated column chromatography over silica gel gave, after the removal of piperine, an oily substance **1**, C<sub>21</sub>H<sub>29</sub>NO<sub>3</sub> by HREIMS. The UV  $\lambda_{\max}$  (260 nm) indicated a chromophoric system similar to piperolein B

(Grewe, Freist, Neumann & Kersten, 1970) and tricholein (Singh, Santani & Dhar, 1976) and the IR (neat) indicated the presence of a tertiary amide ( $\nu_{\max}$  1640 cm<sup>-1</sup>), a *trans* olefinic double bond ( $\nu_{\max}$  963 cm<sup>-1</sup>) and a methylenedioxyphenyl group ( $\nu_{\max}$  1249 cm<sup>-1</sup>, 1039 cm<sup>-1</sup> and 929 cm<sup>-1</sup>).

The 200 MHz <sup>1</sup>H NMR (CDCl<sub>3</sub>) spectrum showed two broad singlets between  $\delta$  1.35–1.50 integrating for 14 protons ( $\beta, \beta'$  protons of pyrrolidine and C-3–C-7 methylenes), a two proton quartet at  $\delta$  2.15 (–CH=CH–CH<sub>2</sub>–), a two proton triplet at  $\delta$  2.30 (–CH<sub>2</sub>–CO–), a two 2 proton triplets at  $\delta$  3.40 and 3.55 ( $\alpha, \alpha'$  protons of pyrrolidine), a two proton singlet at  $\delta$  5.90 (–O–CH<sub>2</sub>–O–), an apparent quartet between  $\delta$  5.95 and 6.15 (–HC=CH–CH<sub>2</sub>–), a doublet at  $\delta$  6.25 ( $J$  = 15 Hz) due to the other olefinic proton and a three proton multiplet between  $\delta$  6.60–7.00 (3 ArH). In the EIMS, fragments, at  $m/z$  161 (7.7%), 131 (56.9%) and 103 (87.7%) suggested a double bond conjugated to the aromatic group (Kiuchi, Nakamura, Tsuda, Kondo & Yoshimura, 1988). These data are in agreement with structure **1**.



The structure of the alkamide was further confirmed

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by alkaline hydrolysis which yielded an oily acid identified as 10-(3,4-methylenedioxyphenyl)-dec-9-enoic acid by its  $^1\text{H}$  NMR and FABMS.

Piperonylic acid and its analogues are generally considered as biogenetic precursors for aromatic piperidine and pyrrolidine alkaloids (Herbert, 1989). The alkaloids so far isolated from *Piper nigrum* are derived from piperonylic acids having aliphatic chain lengths of 3, 5, 7 and 9 carbons, whereas isopiperolein B has an even number (10) of carbons. Hence, its isolation may be biogenetically significant.

### 3. Experimental

#### 3.1. Extraction and isolation

Black pepper (procured locally) was powdered and extracted (Soxhlet) with petrol (60–80°) for 24 h. The petrol extract was filtered to remove piperine and the filtrate was evaporated. The residue was chromatographed twice over silica gel (60–120 mesh) using hexane:EtOAc (9:1) as eluent to give **1** as a yellow oily liquid,  $R_f$  0.60 (hexane:EtOAc 3:1).

Isopiperolein B-HREIMS  $M^+$  343.2135 calcd. for  $C_{21}H_{29}NO_3$ :343.2147.  $^{13}\text{C}$ NMR: (100 MHz,  $\text{CDCl}_3$ )  $\delta$  24.51 (C- $\beta$ ), 25.35 (C- $\beta'$ ), 25.51, 26.49, 28.91, 29.30, 29.70 (C-3–C-7), 32.77 (C-8), 33.37 (C-2), 42.52 (C- $\alpha$ ), 46.64 (C- $\alpha'$ ), 100.80 (–O– $\text{CH}_2$ –O–), 105.95 (C-2'), 108.53 (C-5'), 119.64 (C-6'), 128.00 (C-9), 129.19 (C-10), 132.35 (C-1'), 146.41 (C-3'), 147.80 (C-4'), 171.36 (C-1).

#### 3.2. Hydrolysis of isopiperolein B

Isopiperolein B (30 mg) in saturated KOH solution (1 ml) and MeOH (1.5 ml) was refluxed for 10 h. Water (5 ml) was added and the hydrolysate was washed with EtOAc. The aqueous layer was acidified

with dil. HCl and extracted with ether (2  $\times$  10 ml). The combined extracts were washed with  $\text{H}_2\text{O}$ , dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated leaving a brown oily acid,  $^1\text{H}$  NMR: (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.20–1.35 (10 H, 2bs, 5 methylenes), 2.2 (2H, q, – $\text{CH}_2$ –CH=CH), 2.35 (2H, t, – $\text{CH}_2$ –COOH), 5.90 (2H, s, –O– $\text{CH}_2$ –O–), 5.95–6.15 (1H, q, –CH=CH– $\text{CH}_2$ ), 6.25 (1H, d, –CH=CH– $\text{CH}_2$ –), 6.60–7.00 (3H, m, Ar H); FABMS: ( $M^+$  + Na) 313; IR:  $\nu_{\text{max}}$  (neat): 3088, 2924, 2852, 1707, 1684, 1460, 1445, 1248  $\text{cm}^{-1}$ .

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