

### 3,4-Epoxy-8,9-dihydropiplartine. A New Imide from *Piper verrucosum*

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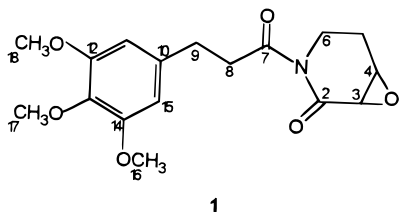
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The structure of a new compound isolated from the leaves and twigs of *Piper verrucosum* Sw. has been established as 3,4-epoxy-8,9-dihydropiplartine (**1**) by spectroscopic methods.

As part of our ongoing work on the phytochemistry of selected species of the endemic Jamaican flora, we have fractionated extracts of the leaves and twigs of *Piper verrucosum* Sw. (Piperaceae), a tree of relatively infrequent occurrence in central Jamaica.<sup>1</sup>

The ground leaves and twigs were extracted with hexanes. The concentrated extract, upon repeated column chromatography and crystallization yielded only 3,4-epoxy-8,9-dihydropiplartine (**1**) (0.0003%). Fractionation and crystallization of the Me<sub>2</sub>CO extract obtained from the marc afforded 3,4,5-trimethoxybenzenepropanoic acid (0.0015%), identified from spectral data and comparison of the mp with the literature value.<sup>2</sup>



Compound **1**, C<sub>17</sub>H<sub>21</sub>NO<sub>6</sub>, mp 85–87 °C, [α]<sub>D</sub> –121.6°, exhibited bands in its IR spectrum that indicated an aromatic ring (1596, 1548, 1473 cm<sup>-1</sup>) and two carbonyl groups (1726, 1698 cm<sup>-1</sup>). The <sup>1</sup>H-NMR spectrum displayed peaks characteristic of a trimethoxybenzenepropanoyl moiety.<sup>3</sup> These consisted of coupled triplets for the C-8 and C-9 methylenes (δ 3.23 and δ 2.91, each 2H, *J* = 7.4 Hz); signals for three methoxyl groups, two of which are equivalent (δ 3.85, 6H, and δ 3.82, 3H), and a shielded aromatic singlet integrating for two protons (δ 6.46). The integration of the latter three signals demonstrated that the aromatic ring is symmetrically substituted as shown. The corresponding carbon signals (see Table 1) were assigned with the aid of HMQC spectra. Cross peaks in the HMBC spectra between both pairs of methylene protons (δ 3.23 and δ 2.91) and a carbon at δ 174.6 established this as the carbonyl of the substituted benzenepropanoyl group. Fragment ions in the EIMS at *m/z* 222, 194, 181, and 179 were consistent with the presence of this group.<sup>4</sup>

<sup>1</sup>H and <sup>13</sup>C signals for the C<sub>5</sub>H<sub>6</sub>NO<sub>2</sub> residue indicated an amidic carbonyl, a disubstituted epoxide, and two methylene groups. HMBC cross peaks between the

**Table 1.** NMR Data of Compound **1** [δ (ppm), CDCl<sub>3</sub>]

position	δ <sub>C</sub>	δ <sub>H</sub> <sup>a</sup>	HMBC <sup>b</sup>
2	169.6		3.56
3	52.3	3.56 (1H, d, <i>J</i> = 4.1 Hz)	3.70, 2.42
4	53.4	3.70 (1H, dd, <i>J</i> = 4.1, 5.8 Hz)	4.34, 2.42
5	23.8	2.42 (1H, m) 2.00 (1H, ddd, <i>J</i> = 15.0, 5.8, 13.2 Hz)	4.34, 3.70
6	35.6	4.34 (1H, dddd, <i>J</i> = 13.5, 5.8, 1.5, 1.5 Hz) 3.20 (1H, m)	2.00
7	174.6		3.23, 2.91
8	41.2	3.23 (2H, t, <i>J</i> = 7.4 Hz)	2.91
9	31.2	2.91 (2H, t, <i>J</i> = 7.4 Hz)	6.46, 3.23
10	136.6		6.46, 3.23, 2.91
11, 15	105.4 (double)	6.46 (2H, s)	6.46, 2.91
12, 14	153.1 (double)		6.46, 3.85
13	136.3		3.82
16, 18	56.0 (double)	3.85 (6H, s)	
17	60.8	3.82 (3H, s)	

<sup>a</sup> Values were established by HMQC. <sup>b</sup> Protons that correlate with carbon resonance.

carbonyl carbon (δ 169.6) and the epoxymethine proton at δ 3.56 demonstrated that the epoxy and carbonyl functionalities are vicinal. Analysis of HMQC, COSY, and HMBC data enabled the complete assignment of the signals for this residue (see Table 1) leading to its formulation as 3,4-epoxy-2-oxopiperdinyll.

The relative stereochemistry was determined from the magnitude of the vicinal coupling between H-3 and H-4 and the results of a NOESY experiment. The *J* value (*J*<sub>3-4</sub> = 4.1 Hz) was exactly as expected for a *cis* coupling with a near-zero dihedral angle in a 1,2-epoxycyclohexane.<sup>5</sup> A *trans* coupling in the same system should have a coupling of ~0 Hz. The NOESY spectrum showed a strong cross peak between H-3 and H-4, again consistent with a *cis* stereochemistry. H-4 showed typical *gauche* couplings along with NOESY cross peaks to both C-5 protons, suggesting that it is in a pseudoequatorial orientation in the six-membered ring. This ring will obviously be distorted from a chair form by the carbonyl and epoxide functionalities.

Compound **1** is a new amide alkaloid and may be regarded as the 3,4-epoxy-8,9-dihydro derivative of the known compound piplartine, which occurs in the roots of the Indian plant *Piper longum* L.<sup>6</sup> A similar compound in which the heterocyclic residue is 3,4-didehy-

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dro-2-oxopyrrolidinyl has been isolated from *Piper demeraranum* (Miq.) C. DC. of Trinidad.<sup>3</sup>

Epoxydes are not common in the *Piper* genus and have been reported only in the Old World species *P. polysyphorum* C. DC. of China and *P. hookeri* Hook, *P. cubeba* (Miq.), and *P. brachystachum* Wall of India. These plants produce the chorismate-derived cyclohexane epoxydes, crotopoxide, and related compounds.<sup>7-9</sup>

### Experimental Section

**General Experimental Procedures.** Melting points were determined on a Thomas-Hoover capillary melting point apparatus. The optical rotation was measured on a Perkin-Elmer 24MC polarimeter. IR spectra were taken on a Perkin-Elmer 735B spectrophotometer as KBr pellets, and the UV spectrum was run on a Pye Unicam 8800 spectrophotometer. MS were obtained on a VG 70-250S mass spectrometer. NMR spectra were determined using a Bruker ACE 200 and a Varian UNITY-500 spectrometer with TMS as internal standard. Column chromatography utilized SiO<sub>2</sub>, Mallinckrodt, 230-400 mesh.

**Plant Material.** The leaves and twigs of *P. verrucosum* Sw. (Piperaceae) were collected near Quickstep, Trelawny, Jamaica, in March 1995. A voucher specimen (no. 33,621) is lodged in the Herbarium at the University of the West Indies, Mona, Jamaica.

**Extraction and Isolation.** Dried leaves and twigs (1.64 kg) were ground and extracted by cold percolation with hexanes. Evaporation yielded a gum (37 g), a portion (12 g) of which was chromatographed (gradient elution with Me<sub>2</sub>CO-hexanes). The residue (1.5 g) from the 20% Me<sub>2</sub>CO fractions was chromatographed in 5% Me<sub>2</sub>CO-hexanes to yield pure **1** (157 mg).

Extraction with cold Me<sub>2</sub>CO of the marc from the hexane extract and evaporation of the solvent gave a

gum (57 g), a portion (12 g) of which was chromatographed (Me<sub>2</sub>CO-hexanes gradient). The fractions eluted with 50% Me<sub>2</sub>CO were rechromatographed, again using a Me<sub>2</sub>CO-hexanes gradient. 3,4,5-Trimethoxybenzenepropanoic acid (500 mg) was obtained from fractions eluted with 25% Me<sub>2</sub>CO-hexanes.

**3,4-Epoxy-8,9-dihydroplartine (1):** Recrystallized from Me<sub>2</sub>CO-ligroin, mp 85-87 °C; [ $\alpha$ ]<sub>D</sub> -121.6° (c 0.020, CHCl<sub>3</sub>); IR  $\nu$  max 1726, 1698, 1596, 1548, 1473 cm<sup>-1</sup>; UV  $\lambda$  max (EtOH) (log  $\epsilon$ ) 260 (2.92) nm; EIMS  $m/z$  [M]<sup>+</sup> 335 (95), 222 (100), 194 (66), 181 (69), 179 (66); HRMS  $m/z$  found 335.1384, calcd 335.1369 for C<sub>17</sub>H<sub>21</sub>O<sub>6</sub>; <sup>1</sup>H and <sup>13</sup>C-NMR data, see Table 1.

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### References and Notes

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