

## A NEW AMIDE FROM *PIPER DEMERARANUM*

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**ABSTRACT.**—The Me<sub>2</sub>CO extract of the aerial parts of *Piper demeraranum* yielded a new dihydrocinnamoyl 2-pyrrolinone amide **1**, the structure of which was determined by spectroscopic methods.

Our continuing interest in the chemistry of the Piperaceae led us to investigate the shrub *Piper demeraranum* (Miq.) C. DC., which occurs in moist, shady regions in Trinidad (1) and has not been previously studied. We wish to report the isolation, from the aerial parts of the plant, of a new dihydrocinnamoyl 2-pyrrolinone amide **1** and three prenylated hydroxybenzoic acids previously isolated from *Piper saltuum* (2).

Compound **1** was isolated after vacuum liquid chromatography (vlc) of the Me<sub>2</sub>CO extract as white needles. Its ir spectrum showed carbonyl absorptions at 1730 and 1690 cm<sup>-1</sup>. Eims gave [M]<sup>+</sup> at *m/z* 305, which is consistent with the molecular formula, C<sub>16</sub>H<sub>19</sub>NO<sub>5</sub>. The <sup>1</sup>H-nmr spectrum indicated a 1-substituted 3,4,5-trimethoxybenzene moiety (6H singlet at δ 3.86, 3H singlet at δ 3.83 and a 2H singlet at δ 6.53). The presence of this moiety was supported by the <sup>13</sup>C-nmr spectrum, which gave signals at δ 153.5, 137.0, and 105.8 (3), and by the mass spectrum, which showed a diagnostic peak at *m/z* 181 (base peak). The two doublets of triplets at δ 7.32 and 6.18 (*J* = 6, 2 Hz) and the related triplet at δ 4.43 (*J* = 2 Hz) suggested the

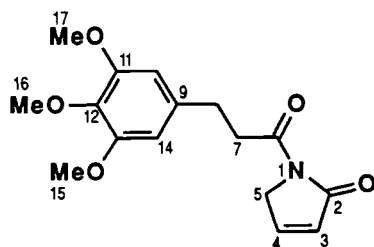
presence of a 5H-2-pyrrolinone ring (4,5) in **1**. This was confirmed by the <sup>13</sup>C-nmr spectrum, which showed signals, at δ 50.4, 128.0, 147.0, and 170.5, that closely corresponded with those reported (5,6) for several 5H-2-pyrrolinones. The two symmetrical 2H multiplets at δ 2.95 and 3.30, the additional carbonyl signal at δ 172.9 in the <sup>13</sup>C-nmr spectrum, and fragment ions at *m/z* 223 and 195 in the eims pointed to the presence of a -CH<sub>2</sub>CH<sub>2</sub>-C=O group linking the aromatic and pyrrolinone moieties. The structure of **1** was therefore formulated as indicated and is in full accord with all the spectral data.

Compound **1** is a novel member of the class of amide alkaloids which is characteristic of the Piperaceae (7,8). A similar compound, piplartine, has been isolated from the roots of *Piper longum* (9). Its dihydro derivative differs from **1** only in the size of the amide ring which is six-membered.

The three acids were obtained after base extraction of the crude Me<sub>2</sub>CO extract followed by workup and preparative layer chromatography (plc) of the isolated mixture. They were shown by uv, ir, and <sup>1</sup>H-nmr spectral comparisons (2) to be, in order of increasing polarity, 3-geranylgeranyl-4-hydroxybenzoic acid, 2-geranylgeranyl-3,4-dihydroxybenzoic acid, and 5-geranylgeranyl-3,4-dihydroxybenzoic acid.

### EXPERIMENTAL

**GENERAL EXPERIMENTAL PROCEDURES.**—Melting points were determined on a Reichert micro mp apparatus and are uncorrected. Uv spectra were recorded on a Perkin-Elmer 552A uv-vis spectrophotometer, and ir spectra were run



**1**

on a Pye-Unicam SP3-200 instrument.  $^1\text{H}$ - (80 MHz) and  $^{13}\text{C}$ - (20 MHz) nmr spectra were run on a Bruker WP 80 SY FT nmr spectrometer with TMS as internal standard. Si gel 60 PF-254 and 366 (Merck) was used for analytical (0.25 mm) and preparative (1 mm) tlc and for vlc (10).

**PLANT MATERIAL.**—Aerial parts of *P. demeraranum* were collected in August 1987 near the 11-mile post along the Arima-Blanchisseuse Road, Trinidad. A voucher specimen is on deposit at the National Herbarium of Trinidad and Tobago. The plant material was air-dried (ca. 30°) for 1 week.

**EXTRACTION, SEPARATION, AND ISOLATION.**—The dried, ground plant material (520 g) was exhaustively extracted with  $\text{Me}_2\text{CO}$  (7 liters) over 5 days. Evaporation of the  $\text{Me}_2\text{CO}$  gave the crude extract (21.4 g). A portion (10 g) of this was subjected to vlc, eluting first with petroleum ether alone and then with petroleum ether/ $\text{Me}_2\text{CO}$  mixtures containing increasing proportions of  $\text{Me}_2\text{CO}$ . Fractions 16–17 yielded **1** as white crystalline needles (38 mg).

**Compound 1.**—Mp 150–151° (petroleum ether/ $\text{Me}_2\text{CO}$ ); uv (MeOH)  $\lambda$  max 264, 213 nm ( $\epsilon$  1300, 21100); ir (Nujol)  $\nu$  max 1730, 1690, 1595, 1510, 1335, 1295, 1252, 1210, 1124, 1008, 848, 815  $\text{cm}^{-1}$ ; eims  $m/z$  (%) [ $\text{M}]^+$  305 (92), 223 (14), 222 (67), 207 (22), 195 (18), 194 (36), 182 (12), 181 (100), 179 (52), 151 (13), 148 (12), 136 (12), 91 (12), 84 (28), 77 (18);  $^1\text{H}$  nmr ( $\text{CDCl}_3$ )  $\delta$  2.95 (m, 2H, H-8), 3.30 (m, 2H, H-7), 3.83 (s, 3H, MeO-16), 3.86 (s, 6H, MeO-

15, 17), 4.43 (t,  $J = 2$  Hz, 2H, H-5), 6.18 (dt,  $J = 6, 2$  Hz, 1H, H-3), 6.53 (s, 2H, H-10, H-14), 7.33 (dt,  $J = 6, 2$  Hz, 1H, H-4);  $^{13}\text{C}$  nmr see Table 1.

A second portion (10 g) of the crude extract was dissolved in  $\text{CHCl}_3$  (100 ml) and extracted twice with NaOH solution (2 M,  $2 \times 75$  ml). The combined aqueous layers were acidified with HCl solution (6 M), and the mixture was extracted with EtOAc. The green residue obtained on evaporation of the solvent was decolorized in  $\text{Me}_2\text{CO}$  solution with powdered charcoal. Filtration and evaporation of the solvent yielded a viscous oil (1.5 g) which after plc [petroleum ether- $\text{Me}_2\text{CO}$  (13:7)] gave three known acids (2) as yellow oils. The least polar of these (51 mg) was shown by comparison of uv, ir, and  $^1\text{H}$ -nmr spectral data to be identical to 3-geranylgeranyl-4-hydroxybenzoic acid. The slightly impure oil of intermediate polarity (64 mg) was converted as described previously (2) to its trimethylated derivative, which proved to be identical (uv, ir, and  $^1\text{H}$ -nmr spectral comparisons) with that of 2-geranylgeranyl-3,4-dihydroxybenzoic acid. Similarly, the most polar acid was shown to be identical with 5-geranylgeranyl-3,4-dihydroxybenzoic acid.

#### ACKNOWLEDGMENTS

The authors wish to thank Mr. M. B. Kalloo of the National Herbarium at our University for kind assistance in the collection and identification of the plant material. We are grateful to Dr. P. S. Manchand, of Hoffmann-La Roche, New Jersey, for the mass spectral data and to the U. W. I. for financial support.

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Received 24 January 1989

TABLE 1.  $^{13}\text{C}$ -nmr data of Compound **1** in  $\text{CDCl}_3$ .<sup>a</sup>

Carbon	Chemical Shift
C-2	170.5
C-3	128.0
C-4	147.0
C-5	50.4
C-6	172.9
C-7	37.8
C-8	30.2
C-9	137.0
C-10	105.8
C-11	153.5
C-12	137.0
C-13	153.5
C-14	105.8
C-15	56.1
C-16	60.5
C-17	56.1

<sup>a</sup>Chemical shifts, relative to TMS, are given in  $\delta$  (ppm). Assignment of the signals was based on the  $J$ -Modulated Spin Echo  $^{13}\text{C}$ -nmr spectrum and comparison of  $^{13}\text{C}$ -nmr data of related compounds (3,6).