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PIRIFERINE, A NEW PYRROLIDINE ALKALOID FROM *AGLAIA PIRIFERA* LEAVES

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ABSTRACT.—The major alkaloid of the leaves of *Aglaia pirifera* (Meliaceae) has been isolated and characterized as a new bis amide of 2-aminopyrrolidine. The new alkaloid, named piriferine [**1**], was identified as *N*-cinnamoyl-2-(2-methylpropanoylamino)-pyrrolidine by analysis of spectral data.

The Thai plant "Kang-Kao" (*Aglaia pirifera* Hance, Meliaceae) is widely distributed in Thailand, especially in the central and northeast regions. The local residents believe that the roots and leaves of this plant can induce vomiting and are useful antidotes for poisoning. Because the plant has not been scientifically tested before, the data on its uses and effects reflect more local lore than empirical observations.

Preliminary screening showed a positive test for alkaloids. *Aglaia* is one of the largest genera of the family Meliaceae. Only two alkaloids have been previously reported and characterized from this genus (1–3).

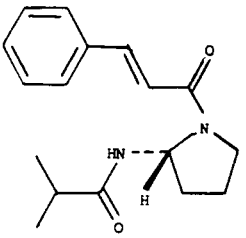
The new alkaloid, named piriferine [**1**] after the specific name of the plant, was identified as *N*-cinnamoyl-2-(2-methylpropanoylamino)-pyrrolidine from spectral data that were compared with those of the known alkaloids, odorine[1] (roxburghilline[2]) [**2**] and odorinol [**3**] (1–3).

The alkaloid shows a molecular ion in the mass spectrum at *m/z* 286.168, indicating a composition of $C_{17}H_{22}N_2O_2$ (calcd 286.168). The result is in agreement with the elemental analysis data, which confirmed the proposed empirical formula. The mass spectral fragmentation pattern (Figure 1) indicates a base peak at *m/z* 131.049 corresponding to the loss of a 2-methylpropanoylamino-pyrrolidine moiety. The strong peaks at *m/z* 215.117, *m/z* 155.118, and *m/z* 71.051 resulted from the loss of isobutanoyl, cinnamoyl, and *N*-cinnamoyl-2-aminopyrrolidine fragments, respectively. In addition, the peak at *m/z* 199.098 corresponds to the loss of 2-methylpropanoylamide via a McLafferty rearrangement (4). This result indicated that a 2-methylpropanoyl moiety was associated with the secondary amide function and, thus, suggested the proposed structure [**1**].

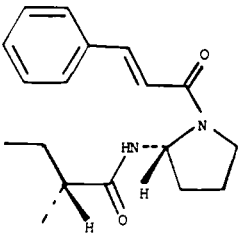
The ir spectrum revealed peaks at 3250 (NH), 1640, and 1610 (amides) cm^{-1}, indicating the presence of secondary and tertiary amides in the molecule. The uv spectrum revealed the presence of cinnamide derivatives. The ^{1}H-nmr spectrum showed that the molecule is a secondary-tertiary bis amide of monocyclic $C_4H_8N_2$ comprising two methylenes, a methylene bearing nitrogen, and a methine bearing two nitrogens. The corresponding ^{1}H-nmr resonances appeared at δ 1.95 (4H, m), 3.46 (2H, m), and 6.13 (2H, t), respectively. The ^{1}H-nmr spectrum also indicated the presence of cinnamoyl [δ 7.30–7.50 (5H, m), 6.83 (1H, d), 7.76 (1H, d)] and 2-methylpropanoyl [δ 1.10 (3H, d), 1.18 (3H, d), 2.50 (1H, m)] residues. The two acid residues and the re-

[1]Isolated from *Aglaia odorata* Lour. (2,3).

[2]Isolated from *Aglaia roxburghiana* Hiern, its structure is apparently the same as odorine (1).



1



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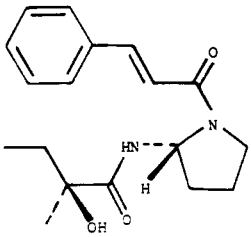

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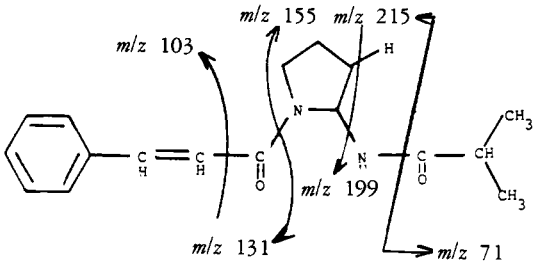

FIGURE 1. Piriferine [**1**] ms fragmentation pattern.

maining carbons were readily identified in the ^{13}C-nmr spectrum. The complete ^{13}C-nmr assignment of **1** was elucidated by comparison with the reported spectrum of odorinol [**3**] (3) as shown in Table 1.

Piriferine differs from odorine and odorinol in that it has only one chiral center, whereas odorine and odorinol each have two. We believe this slight difference does not refute our deduction of the structure by analogy to related molecules. The stereochemistry was not determined; thus, no evidence as to the absolute configuration is

TABLE 1. ^{13}C-nmr Chemical Shift Assignments for Piriferine [**1**] in $CDCl_3$.

Carbon Atom	Pyrrolidine	Cinnamic Acid	2-Methylpropanoic Acid
C-1	—	165.85 (165.86)[a]	176.35 (174.86)
C-2	63.01 (62.52)	142.71 (142.89)	21.73
C-3	34.57 (33.14)	118.49 (118.16)	19.51
C-4	35.54 (34.67)	135.07 (134.98)	—
C-5	46.22 (44.08)	128.89 (128.73)	—
C-6	—	128.24 (128.31)	19.40
C-7	—	129.87 (129.75)	—
C-8	—	128.24 (128.31)	—
C-9	—	128.89 (128.73)	—

[a]Values in parentheses are literature assignments for odorinol (3).

available. Lacking these data, we have drawn the structure in the same 2′*R* configuration that has been assigned to odorine by the optical rotation of its hydrolytic products (5) and to odorinol by its X-ray analysis (3).

As a natural amide, piriferine would not be basic enough to form a salt with picric acid, so the picrate derivative was not attempted. Failure to obtain such derivatives was previously reported by Ungphakorn (6) with odorine and odorinol.

EXPERIMENTAL

PLANT MATERIAL.—*A. pirifera* was collected from the district of Pak-Plee, Nakornnayok Province, in central Thailand in the late fruiting stage on June 6, 1983, by E. Saifah and V. Jongbunprasert. The plant was identified by comparison with voucher specimens at The Botany Section, Technical Division, Department of Agriculture, Ministry of Agriculture and Cooperative, Bangkok, Thailand, where a voucher specimen has been deposited.

EXTRACTION AND CHROMATOGRAPHY.—Leaves of *A. pirifera* were dried in an oven (40–45°) and ground to afford 3 kg of powder. This material was extracted three times for 7-day periods with MeOH (14, 13, and 13 liters). The MeOH extract was concentrated to a syrupy mass and exhaustively extracted with *n*-pentane in a liquid-liquid extractor. The pentane-soluble material (155 g) contained no alkaloids (Dragendorff's) and gave a positive Liebermann Burchard test for steroids but was not further investigated.

The dark MeOH residue was diluted with an equal volume of H_2O. Exhaustive extraction with $CHCl_3$ produced 10 g of alkaloid-positive residue. Chromatography of the 10-g sample on 200 g of Si gel (E. Merck) in a flat bottom column (100 mm i.d.) employing solvent A [$CHCl_3$-EtOAc (7:3)] produced 2.25 g of alkaloid residue.

PIRIFERINE [**1**].—Crystallization of the 2.25-g residue in $Et_2O/CHCl_3$ yielded crystalline **1** (1.90 g, 0.06%), mp 157–158°. Recrystallization from $Et_2O/CHCl_3$ gave **1** (1.55 g), mp 164–165.5°, which exhibited the following properties: $[\alpha]^{28}D$ +30 (*c*=0.01, absolute EtOH); uv max (ε) [EtOH] 283; ^1H nmr (90 MHz, $CDCl_3$) δ 1.10 (d, *J*=8, 3H), 1.18 (d, *J*=8, 3H), 1.95 (m, 4H), 2.50 (m, 1H), 3.46 (m, 2H), 6.13 (t, 1H), 6.83 (d, *J*=14, 1H), 7.30–7.50 (m, 5H), 7.76 (d, *J*=14, 1H); ^{13}C nmr see Table 1; ms *m/z* (%) 286.168 (7), 216.121 (2), 215.118 (11), 199.099 (28), 156.121 (3), 155.118 (38), 132.053 (11), 131.049 (100), 103.054 (37), 102.046 (5), 85.066 (59), 77.039 (18), 71.049 (3), 70.065 (10).

Anal. calcd for $C_{17}H_{22}N_2O_2$, C 71.30, H 7.47, N 9.78. Found: C 71.31, H 7.82, N 9.73.

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