Laurodionine, a New Oxalyl-fused Aporphine Alkaloid from *Phoebe formosana*

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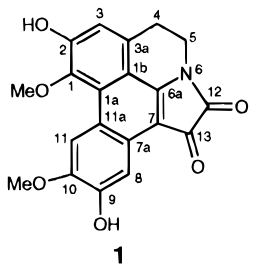
A new aporphine alkaloid, laurodionine (**1**), was isolated from the stems of *Phoebe formosana*, along with *p*-hydroxybenzaldehyde, vanillin, (*E*)-gadain, helioxanthin, *N*-formyldehydroannonaine, and *N*-formylannonaine. The structure of **1** was characterized as N-6/C-7 oxalyl-fused dehydrolaurolitsine by spectral analysis.

Previous studies on *Phoebe formosana* Hayata (Lauraceae), a large plant widely distributed in Taiwan, revealed this species to be rich in aporphine alkaloids, especially the phenolic laurolitsine.[1−3] The present study has focused on the investigation of the neutral, water-insoluble fraction that led to the isolation of a new neutral aporphine alkaloid, laurodionine (**1**), together with six known compounds, that is, *p*-hydroxybenzaldehyde,[4] vanillin,[5] (*E*)-gadain,[6,7] helioxanthin,[8] *N*-formyldehydroannonaine,[9] and *N*-formylannonaine,[10] isolated from the stems. A description of the isolation and structure elucidation of this novel compound follows.

Laurodionine (**1**) was isolated as black prisms, mp >300 °C. The molecular formula of **1**, $C_{20}H_{15}NO_6$, was derived from high-resolution FABMS (negative mode), and from ^{1}H- and ^{13}C-NMR data. The IR absorptions at 1683 and 1727 cm^{-1} indicated the presence of amide and carbonyl groups. Its ^{1}H-NMR spectrum showed three aromatic singlets (δ 8.84, 7.84, and 7.09), two MeO singlets (δ 3.89 and 3.83), and two coupled methylene triplets (δ 3.76 and 3.19, J = 6.4 Hz), identified by double resonance and COSY experiments. These ^{1}H-NMR data indicated that **1** was likely to be a 6a,7-dehydroaporphine like dehydroboldine, except that it lacked the H-7 signal.[11] The absence of an N−Me singlet and H-7 and the presence of additional carbonyl and amide carbons (δ 160.6 and 179.6) suggested that the linkage of a 1,2-dione group was between N-6 and C-7. This proposal afforded an oxalyl-fused dehydroaporphine structure for **1**, like telisatins A and B.[12]



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The position of the 1- and 10-OMe substituents were determined by means of NOE experiments. Both MeO signals were enhanced upon irradiation of H-11 (δ 8.84). Irradiation of the aromatic singlet at δ 7.09 enhanced H-4 (δ 3.19). These results thus confirmed that **1** was 6,7-oxalyl-fused dehydrolaurolitsine, and the trivial name, laurodionine, was given. This is the third natural occurrence of an oxalyl-fused aporphine, the other two being telisatins A and B.[12]

The structure of **1** was supported by its HMBC NMR spectral data, which showed the correlation of the amide carbon (δ 160.6) to H-5 (δ 3.76). Further analysis of this spectrum and the HETCOR spectrum also allowed the complete assignment of the ^{13}C-NMR of **1**.

Experimental Section

General Experimental Procedures. Melting points were measured on a Yanaco micro-melting point apparatus and are uncorrected. The IR spectra were recorded on a BioRad FT-IR spectrometer. ^{1}H- and ^{13}C-NMR spectra were taken on Varian Gemini 200 and Bruker AC-300 (300 MHz) FT-NMR spectrometers. FABMS and EIMS were obtained on a JEOL SX-102A and a JEOL JMS-HX100 spectrometer, respectively.

Plant Material. The stems of *P. formosana* were collected in July 1994 at the garden of the National Research Institute of Chinese Medicine, Taipei, Taiwan. A voucher specimen is maintained in the herbarium of this Institute.

Extraction and Isolation. The air-dried, powdered stems of *P. formosana* (10 kg) were extracted with 95% EtOH (3 × 80 L) at 50 °C. After filtration and evaporation of the solvent under vacuum, the residue was mixed thoroughly with H_2O and divided into H_2O-soluble and H_2O-insoluble portions. The H_2O-insoluble portion was chromatographed on a Si gel (230−400 mesh) column and successively eluted with *n*-hexane−EtOAc (3:1, 2:1, 1:1) and EtOAc to yield four fractions. Fraction 1 was rechromatographed on a Si gel (230−400 mesh) column using a gradient of *n*-hexane−EtOAc (6:1 to 2:1) as eluent to afford helioxanthin (9.2 mg),[8] vanillin (26.3 mg),[5] *p*-hydroxybenzaldehyde (11.5 mg),[4] and *N*-formyldehydroannonaine (7.8 mg).[9] Fraction 2 was subjected to chromatography on a Si gel (230−400 mesh) column and eluted with a gradient of *n*-hexane−EtOAc (5:1 to 1:1) to obtain (*E*)-gadain (14.8 mg)[6,7] and *N*-formylannonaine (21.4 mg).[10] Fraction 4 was further chromatographed with Si gel (230−400 mesh) by using CH_2Cl_2−MeOH (30:1 to 5:1) as eluent to obtain laurodionine (**1**, 20.4 mg).

Laurodionine (1): black prisms (MeOH); mp >300 °C; IR (KBr) ν_{max} 3410 (br), 1727, 1683, 1619, 1556, 1467, 1233 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 204 (4.20), 266

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(4.43), 344 (3.99), 430 (3.73), 537 (3.50) nm; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 3.19 (2H, t, J = 6.4 Hz, H-4), 3.76 (2H, t, J = 6.4 Hz, H-5), 3.83 (3H, s, 1-OMe), 3.89 (3H, s, 10-OMe), 7.09 (1H, s, H-3), 7.84 (1H, s, H-8), 8.84 (1H, s, H-11); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 179.6 (s, C-13), 160.6 (s, C-12), 156.2 (s, C-2), 152.4 (s, C-6a), 148.9 (s, C-9), 146.1 (s, C-10), 143.6 (s, C-1), 131.7 (s, C-3a), 128.8 (s, C-1a or C-7a), 123.1 (s, C-7a or C-1a), 118.2 (s, C-11a), 116.7 (d, C-3), 109.8 (d, C-11), 109.5 (s, C-1b), 107.3 (d, C-8), 101.1 (s, C-7), 59.3 (q, 1-OCH_3), 55.2 (q, 10-OCH_3), 36.2 (t, C-5), 26.5 (t, C-4); HMBC NMR spectral data H-3 to C-1, C-1b, C-2, C-3a, and C-4; H-4 to C-1b, C-3, C-3a, and C-5; H-5 to C-3a, C-4, C-6a, and C-12; H-8 to C-7, C-9, C-10, and C-11a; H-11 to C-1a, C-7a, C-9, C-10, and C-11a; 1-OMe to C-1; 10-OMe to C-10; negative FABMS m/z $[M - H]^-$ 364, 349, 334, 275; HRFABMS (negative) m/z 364.0816 $[M - H]^-$ (calcd for $C_{20}H_{14}O_6N$, 364.0821).

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