

6a,7-DEHYDROBOLDINE FROM THE BARK OF *PEUMUS BOLDUS*

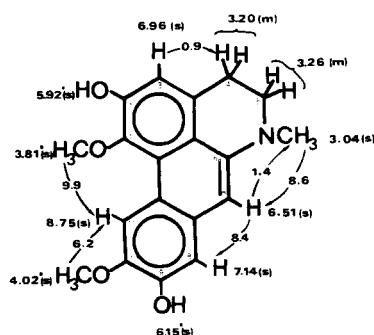
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Peumus boldus Mol. (Monimiaceae), also known as "boldo," is an endemic Chilean tree known for its medicinal properties (1). In addition to boldine, isolated more than 100 years ago, several aporphines and one benzyloisoquinoline have been identified in the leaves (2-4).

Bark of *P. boldus* is exported from Chile for manufacturing the alkaloid mixture (mainly boldine). It has been reported that *P. boldus* bark contains, in addition to boldine, isocorydine, *N*-methyllaurotetanine, norisocorydine, (-)-pronuciferine, and sinoacutine (5).

In this paper, the isolation and characterization of 6a,7-dehydroboldine (**1**), a minor component of the phenolic alkaloid fraction of the bark, is presented.



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The chromatographic separation of the phenolic alkaloid mixture gave a highly unstable fraction. Preparative tlc of this fraction gave a compound that crystallized from EtOH, mp 178-179°, M^+ m/z 325.1284 for $C_{19}H_{19}NO_4$. It showed no optical activity and had an uv spectrum characteristic of a 6a,7-dehydroaporphine (6,7). The bathochromic shift, upon the addition of base, indicated the phenolic nature of the alkaloid. The pmr spectrum was assigned to a

1,2,9,10-tetrasubstituted 6a,7-dehydroaporphine (6,7). Signals at δ 3.04 (s, 3H), δ 3.81 (s, 3H), and δ 4.02 (s, 3H) were assigned to an *N*-methyl and two methoxy groups, respectively. Two broad singlets at δ 5.92 (s, 1H) and δ 6.14 (s, 1H), which disappeared with the addition of D_2O , were assigned to phenolic protons.

The multiplets at δ 3.20 (2H) and δ 3.26 (2H) were assigned to C-4 and C-5 protons, and the singlet at 8.75 (1H) to H-11.

Relative positions of hydroxy and methoxy groups and assignment of the resonances of the aromatic protons were obtained by nmr nOe difference spectra. Irradiation of methoxy singlets at δ 3.81 and δ 4.02 led, respectively, to a 9.9% and 6.2% nOe of the H-11 singlet (δ 8.75), showing that the methoxy groups are situated at C-1 and C-10. Irradiation of the *N*-methyl singlet (δ 3.04) led to a 8.6% nOe of the H-7 singlet (δ 6.51); alternatively, irradiation of the H-7 singlet (δ 6.51) led to a 1.4% nOe of the *N*-methyl singlet (δ 3.04), and 8.4% nOe of the H-8 singlet (δ 7.14). Finally, irradiation of the H-3 singlet (δ 6.96) led to a 0.9% nOe of the C-4 methylene multiplet (δ 3.20).

The compound (4 mg) was treated with Ac_2O and pyridine at room temperature overnight. Work-up in the usual way afforded a pure compound (tlc) that crystallized from MeOH. The compound was identical with synthetic diacetyl-6a,7-dehydroboldine obtained by iodine oxidation of diacetylboldine (8).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined by means of a Kofler hot-stage microscope and are uncorrected.

UV spectra were obtained with a Carl Zeiss DMR-22 spectrophotometer. IR spectra were obtained with a Perkin-Elmer 735-B spectrophotometer. 300 MHz pmr spectra were obtained with a Nicolet NT 300 spectrometer; chemical shifts are reported in δ (ppm) values with TMS as internal standard. High resolution ms were obtained at 70 eV with a Kratos MS-30 mass spectrometer.

P. boldus bark was collected near the summit of Lo Prado Pass, Santiago, Chile, in March (summer), 1981. Voucher specimens have been deposited in the herbaria of the Natural History Museum in Santiago, Chile.

EXTRACTION AND FRACTIONATION.—Powdered, dried bark (1.3 kg) of *P. boldus* was extracted with EtOH, and the alkaloid mixture was fractionated as described previously (5). Boldine (81.6 g), phenolic alkaloid fraction (55.2 g), and nonphenolic alkaloid fraction (2.96 g) were obtained.

The phenolic alkaloid fraction (20 g) was dissolved in CHCl_3 , and chromatographed over a column of silica gel. The column was eluted with CHCl_3 . Each fraction collected was 15 ml.

6a,7-Dehydroboldine (1).—The residue of fractions 27-96 (95 mg), a highly unstable mixture, was subjected to preparative tlc [2 mm silica gel 60 F₂₅₄ chromatoplates, solvent, CHCl_3 -EtOH (98:2)]. Elution of the main band with CHCl_3 -MeOH (9:1) gave a solid (17 mg), mp 178-179° from EtOH; λ max (EtOH) 263 (log ϵ 4.72) and 327 nm (4.06); λ max (EtOH+NaOH) 285 nm (log ϵ 4.83); pmr δ (CDCl_3) 3.04 (s, 3H, N-CH_3), 3.20 (m, 2H, $-\text{CH}_2-$), 3.26 (m, 2H, $-\text{CH}_2-$), 3.81 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 5.92 (s, 1H, OH), 6.15 (s, 1H, OH), 6.51 (s, 1H, H-3), 7.14 (s, 1H, H-8), and 8.75 (s, 1H, H-11); high resolution ms [m/z , composition (%)] 325.1284, $\text{C}_{19}\text{H}_{19}\text{NO}_4$ (100); 310.1059, $\text{C}_{18}\text{H}_{16}\text{NO}_4$ (91).

Acetylation of 6a,7-dehydroboldine (1).—6a,7-Dehydroboldine (1) (4 mg) was reacted with Ac_2O -pyridine at room temperature for 12 h. Work-up in the usual manner gave a solid (4 mg), mp 158-160° from MeOH; ν max (KBr) 1760 cm^{-1} . Identical with an authentic sample of diacetyl-6a,7-dehydroboldine obtained by iodine oxidation of diacetylboldine (8) (mmp, tlc, and ir).

Preparation of diacetyl-6a,7-dehydroboldine from diacetylboldine.—A solution of iodine (0.255 g) in

dioxane (20 ml) was added dropwise over 30 min to a stirred refluxing solution of diacetylboldine (0.344 g) in dioxane (18.5 ml) containing anhydrous NaOAc (0.325 g).

The reaction mixture was cooled, filtered, and evaporated to give a brown residue. The residue was dissolved in CHCl_3 , and chromatographed on a column of silica gel. The column was eluted with CHCl_3 . The residue of fractions 2-6 (0.174 g) was crystallized from MeOH giving diacetyl-6a,7-dehydroboldine (120 mg) mp 159-160°; ν max (KBr) 1760 cm^{-1} ; λ max (EtOH) 246 (log ϵ 4.79), 260 (sh) (4.66), 290 (sh) (4.02) and 333 nm (4.11); pmr δ (CDCl_3) 2.33 (s, 3H, CH_3 -CO-), 2.36 (s, 3H, CH_3 -CO-), 2.96 (s, 3H, N-CH_3), 3.81 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 6.58 (s, 1H, H-7), 7.01 (s, 1H, H-3 or H-8), 7.31 (s, 1H, H-8 or H-3), and 9.00 (s, 1H, H-11).

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¹Diacetyl-6a,7-dehydroboldine has been obtained by photochemical dehydrogenation of diacetylboldine. The mp was 123°. No spectroscopic data have been reported. L. Castedo et al. *Heterocycles*, **15**, 915 (1981).