

(-)-NATALAMINE, AN APORPHINOID ALKALOID FROM
BERBERIS EMPETRIFOLIA

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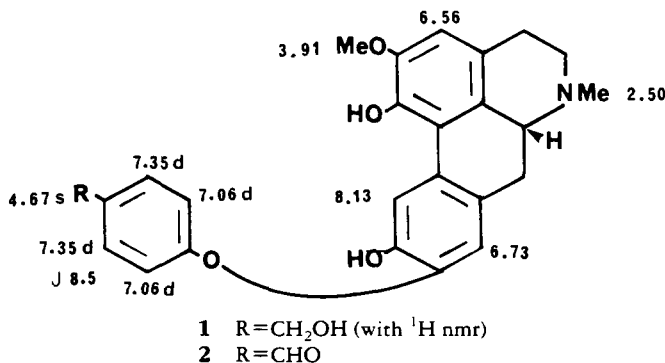
ABSTRACT.—The diphenolic aporphinoid (-)-natalamine [**1**] has been obtained from *Berberis empetrifolia* of Chilean origin.

As part of a continuing study of the alkaloids of Chilean *Berberis empetrifolia* Lam. (Berberidaceae), we had occasion to investigate the content of a fraction obtained by eluting the alkaloids through a column of Si gel using 15% MeOH in CHCl₃. This fraction was found to contain mainly the proaporphine-benzylisoquinoline dimers (+)-patagonine and (+)-valdivianine (1) together with the aporphine-benzylisoquinoline (+)-pakistanine. However, a small spot detected by tlc near the base line [*R_f* 0.08 in CHCl₃-diethylamine (90:10)] turned green with time upon spraying with the chloroplatinic acid reagent (2). This green color suggested the presence of an aporphinoid possessing a C-1 hydroxyl group. The alkaloid was separated by preparative tlc in the same solvent system and purified further by tlc in MeCN-C₆H₆-EtOAc-MeOH-NH₄OH (40:30:20:5:5) to yield 4.3 mg

of natalamine [**1**]: [α]_D -5° (*c* = 0.15, MeOH); λ max (MeOH) 215, 267 sh, 276, 308 nm (log ϵ 4.25, 3.83, 3.77, 3.74); eims *m/z* [*M*]⁺ 419 (C₂₅H₂₅O₅N), 418, 402, 390, 376, 295, 253, 208, 192, 180, 167, 150, 137.

The 200-MHz ¹H-nmr spectrum in CDCl₃, as summarized around expression **1**, is very close to that for the known accompanying alkaloid natalinine [**2**] (3). The main difference lies in the absence of an aldehyde proton in the spectrum of natalamine [**1**], while a two-proton methylene singlet is found at δ 4.76. The cd curve of natalamine [**1**] in MeOH, $\Delta\epsilon_{nm}$ +2.2₂₇₀, -12.9₂₄₁, positive tail near 215 nm, clearly indicates the C-6a *R* configuration, as also evidenced by the negative specific rotation (4).

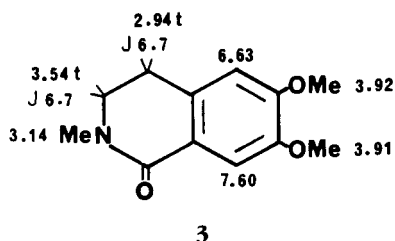
Another alkaloid that we isolated from an earlier fraction of the above column is the known *N*-methylcorydaldine



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[**3**], whose ¹H-nmr spectrum in CDCl₃ at 360 MHz is given around expression **3** [For a review on the isoquinolone alkaloids, see Krane and Shamma (5).] In view of the presence of the aporphine-



benzylisoquinoline dimer (+)-pakistanine in large quantity in *B. empetrifolia*, it is a fair assumption that this alkaloid undergoes in vivo benzylic oxidation to produce *N*-methylcorydaldine [**3**] and (–)-natalinine [**2**]. Natalinine [**2**] could then be reduced in time to (–)-natalamine [**1**]. [For the third review on the dimeric aporphinoid alkaloids, see Guinaudeau *et al.* (6)].

EXPERIMENTAL

PLANT MATERIAL AND EXTRACTION.—*B. empetrifolia* (20 kg of stems and aboveground wood) was collected near Punta Arenas, in southern Chile. A voucher specimen was deposited in the herbarium of the Universidad de Magallanes.

The dried and ground plant material was extracted with EtOH at room temperature. Solvent evaporation was followed by extraction with 5% HCl. The aqueous acid extracts were basified with NH₄OH and extracted with CHCl₃. Evaporation of the CHCl₃ yielded the crude alkaloids. Cc on Si gel, using CHCl₃ gradually enriched with MeOH, was used to separate the alkaloids. Final purification was by tlc on Si gel glass plates.

ACKNOWLEDGMENTS

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