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THE ISOLATION AND SYNTHESIS OF CHANOCLAVINE-I ACID

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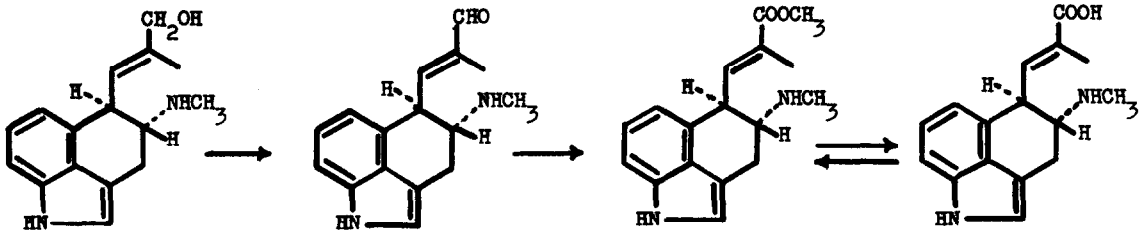
The occurrence of ergoline alkaloids in plants of the Convolvulaceae family is of interest for several reasons including their pharmacological properties and potential value in the chemotaxonomy of these plants. With few exceptions the ergolines isolated from Convolvulaceae are also found in the ergot fungi but there have been a number of reports of unidentified alkaloids in the higher plants.[1,2] Taber, et al.[3] reported that the major alkaloid in the seeds of Ipomea violacea, variety "Pearly Gates," was an ergoline acid which they called "compound A." A substance believed to be this "compound A" has now been isolated and characterized as chanoclavine-I acid (4) and this new secoergoline has been synthesized from chanoclavine-I (1).

Finely powdered seeds[4] (500 g) were defatted, moistened with NH_4OH, and extracted with chloroform which removed nearly all the basic alkaloids.[3] The marc was extracted with MeOH and the extract chromatographed on a column of Amberlite*IR-120; after washing with 80% EtOH the alkaloids were eluted with 3% conc. NH_4OH in 80% EtOH. Thin-layer-chromatography (silica gel G/water) of the eluate showed a non-fluorescent, Ehrlich-positive (blue) alkaloid (rf 0.43) and only traces of other compounds. Final purification by preparative-tlc provided, after recrystallization from MeOH, 50 mg of white crystals, m.p. 245-247° (dec.).

The isolated alkaloid was characterized as chanoclavine-I acid (4) on the basis of both its physical and chemical properties. The mass spectrum showed a molecular ion of m/e 270 along with prominent peaks at 252, 197, 168, 167, 155, and 154.[5] The ir spectrum of the HCl salt showed strong absorption at 1700 cm^{-1} indicative of the -CH=C-COOH and the pmr spectrum (DMSO-d_6) was similar to that of chanoclavine-I (1)[6] except for the absence of the $-CH_2OH$ absorption and the presence of a singlet at δ 11.1 (-COOH). Compound 4 was readily converted (MeOH/HCl/0°) to the methyl ester 3 and $LiAlH_4$ reduction of both 3 and 4 afforded chanoclavine-I (1).

For the synthesis of chanoclavine-I acid (4) the aldehyde 2 was prepared by MnO_2 oxidation[7,8] of 1 obtained by the method of Acklin, et al.[10] Direct oxidation of 2 with permanganate,

dichromate, and silver oxide led to extensive decomposition and gave only traces of 4. However, 2 could be converted to 3 in about 30% yield by cyanide-catalyzed MnO_2 oxidation in MeOH.[11] Hydrolysis (1 N NaOH/90°) of 3 provided chanoclavine-I acid (4) in 80% yield and this compound was identical (tlc, m.p., uv, ir, pmr, mass spectra) to the alkaloid obtained from the "Pearly Gates" seeds.



1 2 3 4

Chanoclavine-I acid was heretofore unknown, however, the rugulovasines derived from Penicillium spp. can be considered to be isochanoclavine acid derivatives.[12] The discovery of chanoclavine-I acid in Ipomea violacea raises several interesting questions concerning its biosynthesis and possible occurrence in other ergoline-producing organisms.

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