

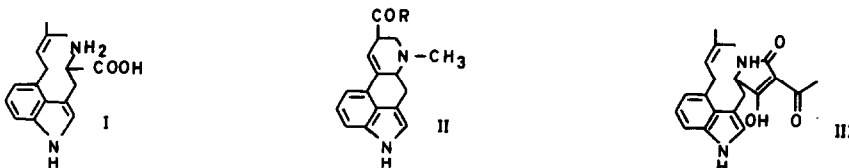
NATURAL OCCURRENCE OF 4-DIMETHYLALLYLTRYPHTOPHAN-AN ERGOT ALKALOID PRECURSOR^a

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The biosynthetic steps involved in the formation of the ergoline skeleton and the transformations of the ergot alkaloids are generally well known (cf.1). The ergoline skeleton (II) is formed from tryptophan and an isoprene unit derived from mevalonic acid. Hypothetically tryptophan may be alkylated in the 4-position of the indole nucleus (I) or on the α -carbon of the alanine side chain. 4-Dimethylallyltryptophan (I) has so far not been isolated from nature but is known to be an efficient precursor of both clavine type and lysergic acid type (II) ergot alkaloids (2,3).



In this paper we report the natural occurrence of 4-dimethylallyltryptophan(I) in a Pennisetum type ergot strain producing mainly elymoclavine (4).

Experimental. - The ergot culture was grown on 500 ml of a glucose-mannose medium in 2.5 l Fernbach flasks (4) as still cultures. After 18 days of growth the medium was supplemented with 25 mg tryptophan and 80 mg ethionine per flask. Two days later the mycelia were harvested and homogenized in 50% aqueous methanol. The filtered extract was evaporated to a small volume, freed from alkaloids by chloroform extraction (4) and applied to a column of Sephadex G 25 Fine (2 x 180 cm), which was eluted with water (25 ml/h). Aromatic compounds are retained by the Sephadex matrix and I and tryptophan have a ret. vol. approx. 2.5 x ret. vol. of glucose as shown by model experiments. The fractions possible

a) Part II of Identification of alkaloid intermediates by gas chromatography-mass spectrometry. Full details to be published later.

ly containing I were pooled and lyophilized. This fraction was methylated and trifluoroacetylated as described for amino acids (5) and subjected to gas chromatography (Aerograph 204) on a column of 5% SE-30 on Gas Chrom P (initial temp. 130°, program. at 4°/min. to 250°; or 180° isothermal). A peak corresponding to reference TFA-4-dimethylallyltryptophan methyl ester was present. By gas chromatography - mass spectrometry (LKB 9000 Instrument) this peak was found to have a mass spectrum identical with that of authentic material (Fig. 1).

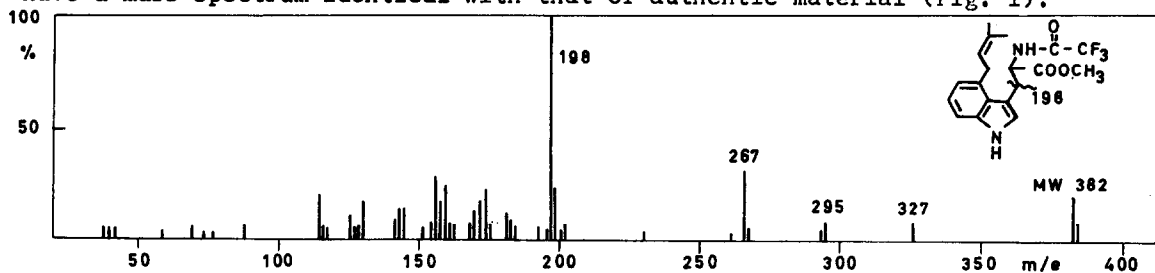


Fig. 1. Mass spectrum of TFA-4-dimethylallyltryptophan methyl ester.

In connection with the here demonstrated occurrence of 4-dimethylallyltryptophan in nature^b it may be mentioned that a very closely related compound, β -cyclopiazonic acid (III) has been discovered (6) in a Penicillium species; a genus where also ergot alkaloids are known to occur (cf.1).

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^{b)} I appears to have been identified in ergot also by Robbers et al., Abstracts of Meeting of American Society of Pharmacognosy, The University of Iowa, Iowa, July 1968.