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A NATURALLY-OCCURRING ALLENIC AMINO ACID

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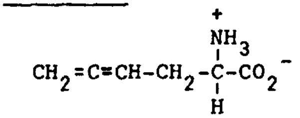
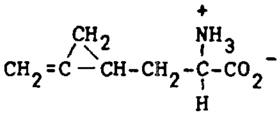
The mushroom genus Amanita is a source of a number of exotic amino acids both in the free amino acid pool (1) and in toxic cyclic peptides (2). We now report the isolation and structure of a naturally-occurring allenic amino acid (I) from A. solitaria.



$CH_2{=}C{=}CH{-}CH_2{-}\overset{\overset{+}{NH_3}}{\underset{H}{C}}{-}CO_2^-$

I



II

Two dimensional chromatograms of aqueous-ethanolic extracts of A. solitaria (Fr.) Secr sensu D. E. Stuntz showed the presence of a new amino acid chromatographically and electrophoretically indistinguishable from valine in position but distinguished by a permanent brown ninhydrin reaction characteristic of unsaturated amino acids. The amino acid is destroyed by bromine, potassium permanganate and prolonged treatment with hydrochloric acid or dilute sodium hydroxide. The amino acid was isolated by extraction of A. solitaria with 70% ethanol followed by elution of the amino acid complex from cellulose with butanol-acetic acid-water 4:1:5. Fractions containing the amino acid, R_f 0.54, and small amounts of valine were rechromatographed until free of valine. The amino acid was crystallized from methanol by Soxhlet extraction. It darkens above 200° without melting. Its infrared spectrum showed, in addition to bands characteristic of the amino acid zwitterion (3300 cm^{-1}, 2400 cm^{-1}, 2100 cm^{-1}, 1600 cm^{-1}) a strong band at 1930 cm^{-1} assigned to an allene and at 850 cm^{-1} assigned to the methylene of a terminal allene. The nmr spectrum of the zwitterion in D_2O is consistent with structure I: three allenic hydrogens, 4.8 - 5.4 τ, multiplet; one α-methine hydrogen, 6.30 τ, doublet of doublets; two α-methylene

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hydrogens, 7.56 τ, multiplet. The chemical shifts may be changed by changing the degree of protonation of the amino and carboxyl groups. The increased shielding attending changing pH from 1 to 11 falls off with distance from the amino and carboxyl groups: α-methine +0.9 ppm, β-methylene +0.4 ppm, and less than 0.1 ppm for the γ and ε allenic hydrogens. The methine hydrogen signal appears as a doublet of doublets coupled to the non-equivalent methylene hydrogens. The allenic hydrogen signals are rendered complex by the long range allenic coupling to the β-methylene hydrogens. The non-equivalent β-methylene hydrogens are coupled to every non-exchangeable hydrogen in the molecule giving rise to an unresolved multiplet.

The allenic amino acid is reduced catalytically to a single substance with uptake of 2.0 moles of hydrogen. The tetrahydroamino acid produced lacks the allene band in the IR spectrum and is chromatographically indistinguishable from leucine, norleucine and isoleucine. Its nmr in D_2O and trifluoroacetic acid is identical to that of norleucine and distinct from those of leucine and isoleucine. Acetylation of the tetrahydroamino acid gave racemic N-acetyl norleucine, mp 104°, $C_8H_{15}NO_3$ (mass spectrometric and combustion analyses).

Although inactive at the sodium D line, the allenic amino acid is dextrorotatory at short wavelength in hydrochloric acid. The norleucine derived by hydrogenation is much more strongly dextrorotatory, $[\alpha]_D^{23}$ 12 (c 1, 5 N HCl). Enzymatically resolved L-norleucine is dextrorotatory in hydrochloric acid (3). Hence the allenic amino acid is 2(S)-amino-4,5-hexadienoic acid.

The reported physical properties of synthetic I (4) are identical to those of the naturally-occurring amino acid. An intermediate in the synthesis of I has been converted into hypoglycine A (II) by carbene addition (4). Hypoglycine A has been found in a higher plant (5) but not in mushrooms.

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