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CYCLOPROPYLALANINE, AN ANTIFUNGAL AMINO ACID OF THE MUSHROOM AMANITA VIRGINEOIDES BAS

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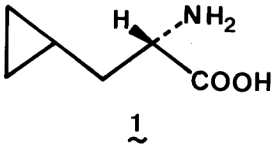
Cyclopropylalanine, an antifungal amino acid, has been isolated from the mushroom Amanita virgineoides Bas. Its structure has been elucidated as (2S)-2-amino-3-cyclopropylpropionic acid, on the basis of the spectroscopic analysis and its synthesis from L-allylglycine.

During the investigation of biologically active components of fungi, we have found that an unusual amino acid of Amanita virgineoides Bas, at 31.3 μg/ml, inhibits the spore germination of Pyricularia oryzae Cav. which causes rice blast disease. The present communication describes structural elucidation and synthesis of the amino acid for which the term cyclopropylalanine is proposed.

The amino acid (198 mg), mp 240 °C (decomp, sublimes on heating), $C_6H_{11}NO_2$,[1] and $[\alpha]_D$-12.4° (c 0.13, H_2O), was isolated from neutral and acidic amino acids of the fruit-bodies (243 g) of A. virgineoides, by chromatography on Dowex 50W. The column was buffered with 0.2 M ammonium formate, pH 3.02, and the amino acids were eluted with the same buffer. The NMR spectra indicated that a monosubstituted cyclopropane ring [δ_H 0.16 (2H, m), 0.54 (2H, m), 0.73 (1H, m); δ_C 4.5 (t, J=160.4 Hz), 4.9 (t, J=160.4 Hz), 7.2 (d, J=154.8 Hz)] has a vicinal methylene [δ_H 1.79 (2H, m); δ_C 36.0 (t, J=128.4 Hz)], which is adjacent to a methine [δ_H 3.80 (1H, dd, J=5.6, 6.5 Hz); δ_C 56.3 (d, J=144.0 Hz)]. The presence of a carboxylate was



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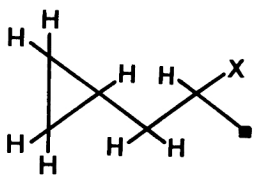
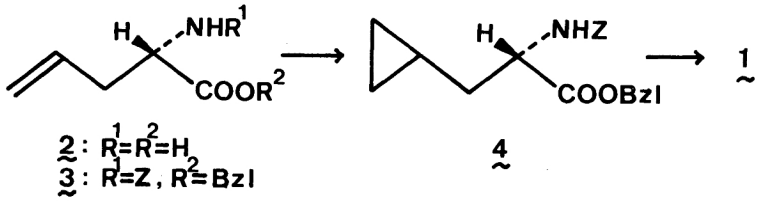


implied by ^{13}C signal at δ 175.1 (s) and by ir absorption at 1580 cm^{-1}. On Adams platinum catalyst, this amino acid was hydrogenated slowly, at 60-65 °C, to leucin and norleucine (ca. 8:3).

The above partial structure and the chemical transformation led to the conclusion that the amino acid is represented as 2-amino-3-cyclopropylpropionic acid 1.[2] CD sign of 1 ($[\theta]_{204}$ + 2070) denotes (2S)-configuration of this amino acid.[3] This assignment was supported by the fact that cyclopropylalanine (1) was oxidized completely with L-amino acid oxidase of Habu snake venom.[4]

The stereostructure 1 was also determined by the synthesis of L-cyclopropylalanine (1) from commercially available L-allylglycine (2)[5] as follows.[6] Benzyl N-benzyloxycarbonyl-L-allylglycinate (3) which was prepared from amino acid 2 in 77% yield, was refluxed with CH_2I_2 (5 equiv.) and copper powder (10 equiv.) in benzene-toluene (1:1) for 1.5 d.[7] Cyclopropyl product 4 (50%) was separated from the starting material 3 (31%), on silica gel coated with 10% silver nitrate, with benzene elution. Hydrogenolysis of 4 gave (2S)-2-amino-3-cyclopropylpropionic acid (1) quantitatively, mp 240 °C (decomp), $[\alpha]_D$-13.4 °C (c 0.11, H_2O). The synthesized amino acid (1) was identical with natural cyclopropylalanine by spectral comparison (MS, IR, and ^1H NMR).



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References

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2) (±)-1 has been synthesized as an antagonist to E. coli: J. S. Meek and J. W. Rome, J. Am. Chem. Soc., 77, 6675 (1955).
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