FORMATION OF β-METHYLDEHYDROALANINE IN THE MILD ALKALINE TREATMENT OF THE ANTIBIOTIC PEPTIDOCYCLOLACTONE A-128-OP

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The antibiotic A-128-OP is a tripeptide-octacyclolactone, the lactone bond in which is formed through the carboxy group of L-cis-3-hydroxyproline and the hydroxy group of L-threonine [1-3]. In addition to L-threonine, the antibiotic contains other hydroxy amino acids: D-allothreonine, D-serine, trans-3-hydroxyproline, and erythro-β-hydroxyleucine.

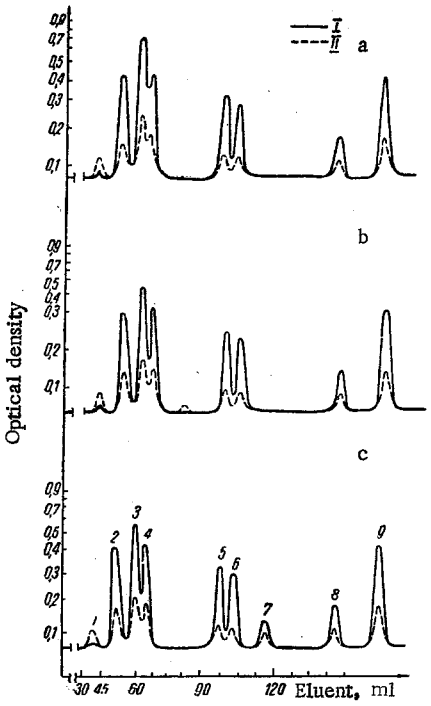

Fig. 1. Amino-acid composition of acid hydrolysates at optical densities of 570 (I) and 440 nm (II): a) antibiotic A-128-OP; b) antibiotic A-128-OP treated with 0.1 N NaOH; c) antibiotic A-128-OP after treatment with 0.1 N NaOH and hydrogenation over Pd/C. 1) trans-3-Hydroxyproline; 2) aspartic acid; 3) threonine, allothreonine, and cis-3-hydroxyproline; 4) serine; 5) glycine; 6) alanine; 7) α-aminobutyric acid; 8) erythro-β-hydroxyleucine; 9) norleucine (standard).

The mild alkaline hydrolysis of the antibiotic (0.1 N NaOH, 37° C, 1 h, or 5% solution, 20° C, 0.5 h) gave a linear 11-membered polypeptide with C-terminal L-cis-3-hydroxyproline (acid of the antibiotic A-128-OP) which migrated to the anode on electrolysis in a buffer with pH 6.5.

On qualitative and quantitative amino-acid analysis of an acid hydrolysate of the acid of the antibiotic A-128-OP there was no L-threonine participating by its OH group in the formation of a lactone bond. Since it is known that some O-derivatives of serine undergo β-elimination on treatment with alkaline agents with the formation of dehydroalanine [4-6], we assume that such elimination takes place in the alkaline treatment of the antibiotic A-128-OP. As a result of β-elimination, L-threonine gives β-methyldehydroalanine, which decomposes in a similar manner to dehydroalanine [7, 8] on acid hydrolysis. The presence of β-methyldehydroalanine in the A-128-OP acid was shown by two methods.

1. The acid of the antibiotic was hydrogenated over a Pd/C catalyst, after which the β-methyldehydroalanine had been converted into α-aminobutyric acid. The latter was identified in the hydrolysate of the reduced A-128-OP acid by thin-layer chromatography and electrophoresis and on a "Hitachi" type KLA-3B automatic amino acid analyzer (Fig. 1).

2. It is known that sodium sulfite adds quantitatively to the double bond of dehydroalanine forming cysteic acid [9]. The action of sodium sulfite on the acid of the antibiotic gave a substance with a higher mobility to the anode on electrophoresis in electrolytes with pH 2.4 and 6.5 than the initial A-128-OP acid. This

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shows the addition of a SO_3H grouping to the double bond of the dehydro amino acid. In addition to this, in an acid hydrolysate of the SO_3H derivative of the A-128-OP acid an amino acid was found with electrophoretic and chromatographic properties close to those of cysteic acid.

Thus, the results given show that β-methyldehydroalanine is formed in the mild alkaline treatment of the antibiotic peptidocyclolactone A-128-OP.

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