THE STRUCTURE OF ISARIIN

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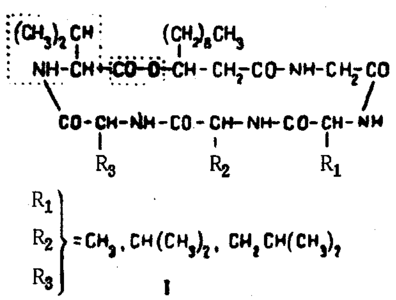
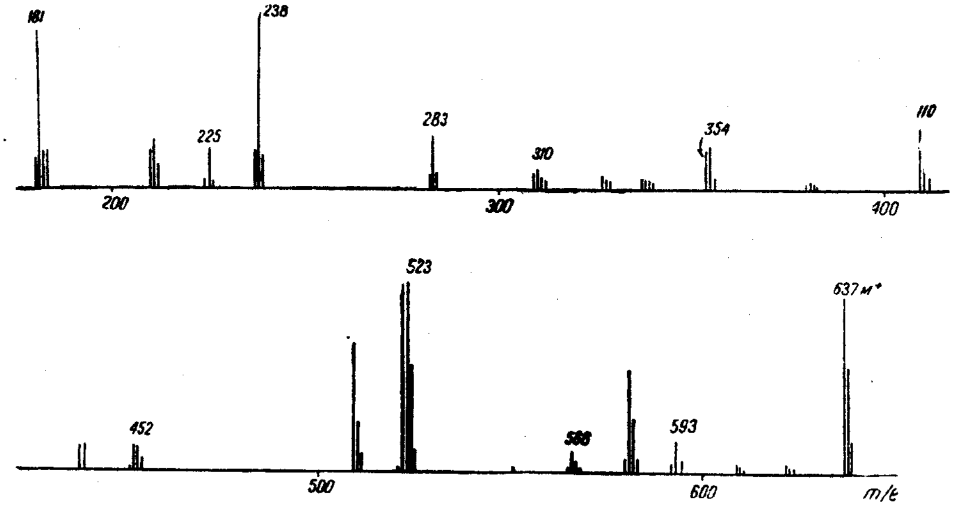
Isariin was isolated in 1962 by Vining and Taber from the metabolic products of the fungus Isaria cretacea [1]. The results of a study of the products of the chemical degradation and the physicochemical data enable the partial formula (I) to be assigned to this substance:



I

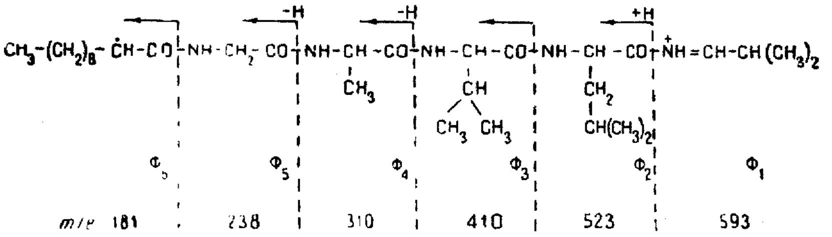
Isariin is a cyclic hexadepsipeptide constructed of one residue of D-β-hydroxydodecanoic acid and five amino acid residues (glycine, two L-valine residues, L-alanine, and D-leucine), the sequence of three of them being undetermined.



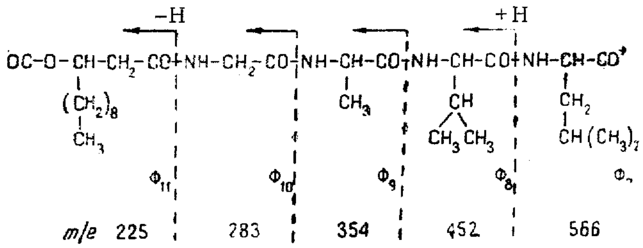
Mass spectrum of isariin.

In order to establish the sequence of the D-leucine, L-valine, and L-alanine residues in the isariin molecule, we have made use of the method of mass spectrometry which, as we have shown previously, enables the sequence of amino acid residues in peptides and depsipeptides to be determined [2].

We may consider two independent routes of the degradation of the molecular ion of isariin: the CO_2 [3] and the imine [4] types of fragmentation (figure). The first mode of degradation begins with the elimination of CO_2, which leads to the appearance of the radical ion Φ_1 (m/e 593). Further degradation of the fragment Φ_1 is associated with the successive rupture of amide bonds accompanied by the splitting off of amino acid residues and the formation of the fragments $\Phi_2-\Phi_6$:

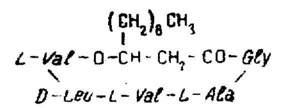


The rupture of the amide bonds may be accompanied by the migration of a hydrogen atom (+ H above an arrow denotes the migration of a hydrogen atom to the residual fragment, and −H the reverse migration). The fragment Φ_2 contains 3 amino acid residues (leucyl, valyl, and analyl) whose sequence is to be determined. The mass spectrum of isariin has two peaks (m/3 410 and 542). Their appearance may be explained by the elimination from Φ_2 of residues of leucine (m/e 410) or of alanine (m/e 452). Taking into account Vining's results on the decomposition of isariic acid by carboxypeptidase [1], it must be assumed that leucine is in fact eliminated from Φ_2 with the formation of the fragment Φ_3 (m/e 410). The peak with m/e 452 corresponds to the fragment Φ_8; its structure is given below. The question of which amino acid residue (that of valine or that of alanine) is connected with the leucine residue (peaks with m/e 339 and 310 are found in the mass spectrum) is decided by a consideration of the imine type of fragmentation. The latter begins with the removal of the imine fragment of valine [$NH{=}CH{-}CH(CH_3)_2$], the residue of which is directly bound to the residue of the β-hydroxydodecanoic acid. This gives rise to the radical ion Φ_7 (m/e 566). Its further decomposition takes place by the successive rupture of amide bonds with the formation of the fragments $\Phi_8-\Phi_{11}$:



If the alanine residue was attached to the leucine residue, a peak with m/e 381 should correspond to the Φ_9 fragment, but this is practically absent from the mass spectrum of isariine (see figure).

Consequently, the following sequence is the most likely: leucyl ← valyl ← alanyl, and therefore the structure of isariine should correspond to formula (II):



II

Summary

On the basis of an analysis of the mass spectrum of isariin it has been shown that the latter has the structure expressed by formula (II).

REFERENCES

1. L. C. Vining and W. A. Taber, Can. J. Chem., 40, 1579, 1962.
2. N. S. Vul'fson, et al., Tetrah., Lett., No. 32, 2805, 1965.
3. N. S. Vul'fson, et al., Tetrah., Lett., no. 17, 951, 1964.
4. B. J. Willard, Tetrah. Lett., no. 34, 3041, 1965.

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