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MASS SPECTROMETRIC STUDY OF CYCLODEPSIPEPTIDES. STAPHYLOMYCIN S

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PREVIOUSLY we have shown (1-5) that the mass spectrometric method can be successfully used for rapid determination of cyclic di-, tetra- and hexadepsipeptide structures with various sequences of amino and hydroxy acid residues. Each of these cyclodepsipeptide groups is characterized by a specific type of fragmentation which is usually a predominant one, thus facilitating elucidation of cyclodepsipeptide structure. At the same time mass spectra of sterically unhindered cyclodepsipeptides with larger ring size, for example, cycloocta- and cyclododecadepsipeptides, are difficult to interpret (6). This is due to the practically equal probability of rupture of various ester and amide bonds under electron impact. For the same reason the occurrence of various types of fragmentation often precludes or makes difficult amino acid sequence determination of cyclic peptides (7).

In our opinion, the mass spectrometric behavior of cyclic depsipeptides containing only one ester bond should be quite different because in these cases one can expect the first act of fragmentation to be rupture of the ester bond. In order to verify this assumption we studied mass spectrometric behavior of staphylomycin S (I)*, in which there is a lone ester bond formed

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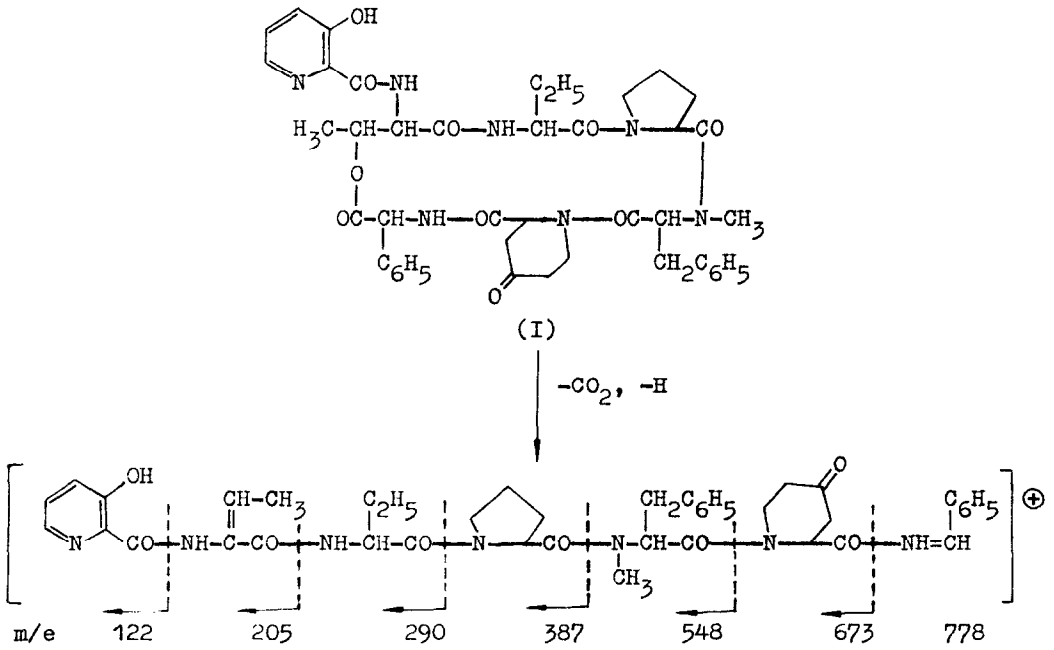
by the hydroxyl group of a threonine residue. In addition, the mass spectrum of this compound provides a further possibility for testing the universality of the amino acid type of fragmentation on which is based the amino acid sequence determination of peptides. This method had been studied heretofore mainly on peptides containing the ordinary amino acid residues (8) whereas four of the six amino acids in the staphylomycin S molecule (α-aminobutyric acid, N-methylphenylalanine, 4-ketopipecolic acid and phenylglycine) are not found in proteins.

The mass spectrum of staphylomycin S (FIG. 1) exhibits a rather intense peak due to the molecular ion (m/e 823), whose first act of fragmentation is in fact elimination of the elements of the ester group (CO_2 type of fragmentation (4)). The resultant linear fragment is stabilized by elimination of a hydrogen atom from the threonine residue with its conversion into a α,β-unsaturated amino acid residue. This is followed by stepwise elimination of the amino acid residues:



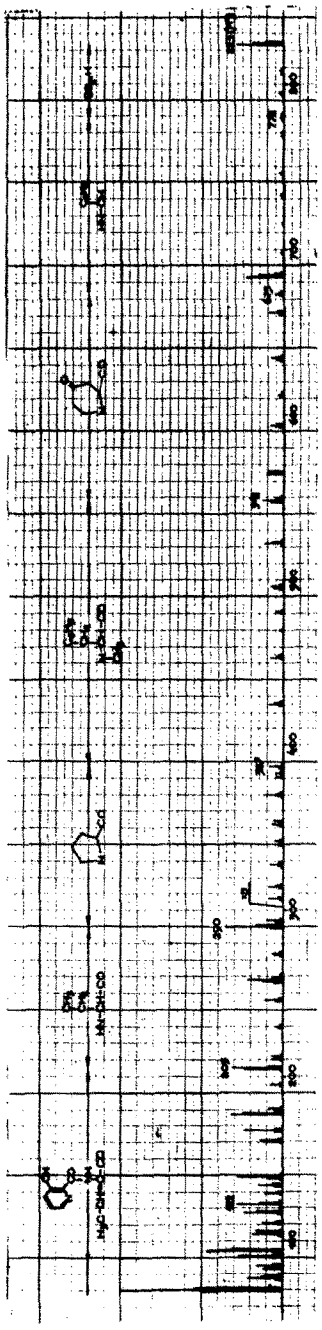


FIG. 1. Line drawing of the mass spectrum of staphylomycin S taken on a commercial RMU-6D (Hitachi) instrument at 280° with the sample introduced directly into the ion source

In this case the amino acid type of fragmentation is predominant confirming the structure (I) suggested for staphylomycin S (9). Of course, the amino acid type of fragmentation does not exhaust all the specific features of the mass spectrometric behavior of this antibiotic. A detailed analysis of the various types of fragmentation undergone by staphylomycin S and related antibiotics will be given elsewhere.

The data presented here clearly show how the mass spectrometric method of the amino acid sequence determination can simplify and accelerate the structure elucidation of such compounds.

REFERENCES

1. N.S.Wulfson, V.A.Puchkov, V.N.Bochkarev, B.V.Rosinov, A.M.Zyakoon, M.M.Shemyakin, Yu.A.Ovchinnikov, V.T.Ivanov, A.A.Kiryushkin, E.I.Vinogradova, M.Yu.Feigina and N.A.Aldanova, Tetrahedron Letters 1964, 951.
2. M.M.Shemyakin, V.A.Puchkov, N.S.Wulfson, V.N.Bochkarev, Yu.A.Ovchinnikov, A.A.Kiryushkin, V.T.Ivanov, E.I.Vinogradova and M.Yu.Feigina, Izv. Akad. Nauk SSSR, Ser. Khim. 1966, 1539.
3. V.N.Bochkarev, V.A.Puchkov, N.S.Wulfson, M.M.Shemyakin, Yu.A.Ovchinnikov, A.A.Kiryushkin, V.T.Ivanov, E.I.Vinogradova and N.A.Aldanova, Khimiya Prirodnykh Soedinenii 1, 52 (1965).
4. N.S.Wulfson, V.A.Puchkov, B.V.Rosinov, A.M.Zyakoon, M.M.Shemyakin, Yu.A.Ovchinnikov, A.A.Kiryushkin and V.T.Ivanov, Tetrahedron Letters 1965, 2793.
5. N.S.Wulfson, V.A.Puchkov, B.V.Rosinov, Yu.V.Denisov, V.N.Bochkarev, M.M.Shemyakin, Yu.A.Ovchinnikov, A.A.Kiryushkin, E.I.Vinogradova and M.Yu.Feigina, Tetrahedron Letters 1965, 2805.
6. B.V.Rosinov, Thesis, Moscow, 1966.
7. A.Prox and F.Weygand, Report to the 8th European Peptide Symposium, Noordwijk, Holland, 1966.
8. M.M.Shemyakin, Yu.A.Ovchinnikov, A.A.Kiryushkin, E.I.Vinogradova, A.I.Miroshnikov, Yu.B.Alakhov, V.M.Lipkin, Yu.B.Shvetsov, N.S.Wulfson, V.N.Bochkarev, B.V.Rosinov and V.M.Burikov, Nature 211, 361 (1966).
9. H.Vanderhaeghe and G.Parmentier, J. Am. Chem. Soc. 82, 4414 (1960).