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chemical structures A, B, V

Figure 1: chemical structures A, B, V

mass spectrum

Figure 2: mass spectrum

Abstract

Full Text

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STUDY OF THE MUTUAL TRANSFORMATIONS OF CYCLOLS AND CYCLODEPSIPEPTIDES BY THE METHOD OF FRAGMENTATION MASS SPECTROMETRY

Earlier (*1*) we showed the possibility of converting N-oxyacyl lactams (A) into oxacyclols (B) and cyclodepsipeptides (V).

For further study of the problem of mutual transitions $A \rightleftarrows B \rightleftarrows V$, the application of the method of fragmentation mass spectrometry proved very fruitful, since the principal differences in the structure of compounds of types A, B, and V are manifested quite specifically in their mass spectra. With the aid of this method we were able not only to obtain new unambiguous evidence for the structures of the cyclols (Ia–g) and cyclodepsipeptides X and XIX, but also, using compounds Ia,b and X as examples, to detect the possibility of mutual transformations of cyclol and cyclodepsipeptide structures under the conditions of mass spectrometry (Ia,b $\rightleftarrows$ II; X $\rightleftarrows$ XI), although under ordinary conditions these compounds are not inclined to pass into one another (*1*). The data obtained by us confirm, in particular, the conclusion regarding the presence of a transannular interaction in cyclodepsipeptide (X), which manifests itself under the action of electron impact in the form of a transannular reaction (X $\rightarrow$ XI). The mass spectra were obtained on an MX-1303 instrument with an inlet system made of stainless steel, at a temperature of about 125° and an ionizing voltage of 25–40 eV.

Fig. 1

As is evident from scheme 1 and Figs. 1–3, a characteristic direction of fragmentation of cyclols (Ia–g) is the elimination of water or methanol elements from

Fig. 2

Figure 3: Fig. 2

the molecular ion. The intensity of the latter in the case of cyclols (Ia,b,g) is extremely small (for Ib the M^+ peak is absent altogether), whereas the peaks with m/e $M-18$ or $M-32$ are the most intense in the spectra. Further fragmentation of ions with m/e $M-18$ or $M-32$ (fragment III) leads stepwise to peaks with m/e 83 and 81, characteristic of cyclols (Ia,v) (fragments Va and VIa), whereas cyclols (Ib,g) give, respectively, peaks with m/e 97 and 95 (fragments Vb and VIb). In contrast to cyclols, in the spectrum of cyclodepsipep-

Scheme 1

[chemical fragmentation scheme]

peptide XIX, which is not capable of cyclol formation, has a noticeable molecular peak, whereas the peak at m/e $M-18$ is very insignificant. The fragmentation of this compound is characterized by formation of the caprolactam ion XX with m/e 113.

A typical feature of compound X is the transannular interaction of its ester and amide groups, by which it differs from other cyclodepsipeptides having a larger ring size. Therefore, it could be expected that the spectrum of this cyclodepsipeptide would contain not only peaks of fragments arising from the macrocyclic form, but also fragments corresponding to the cyclol form (XI), the formation of which should be the result of a transannular reaction. Indeed, in the spectrum of X there is an intense peak at m/e 99 (the valerolactam ion; see Fig. 4), while in the spectrum of XIX, in which transannular interaction is absent, there is a peak at m/e 113, corresponding to the caprolactam ion. However, the spectrum of X also contains peaks at m/e 153 (fragment XII), m/e 125 (fragment XIII), m/e 97 (fragment XIV), etc., characteristic of the fragmentation of the cyclol form (XI), which arises under mass-spectrometric conditions. It should be noted that the difference in the structures of fragments (XIII) and (IVb) with m/e

125, arising from compounds (Ib,d) and (X), is evidently due to a change in the ring size in the molecular ions of the corresponding cyclol forms. Along with this, cyclodepsipeptide X, under electron impact, forms a fragment with m/e 114, having the structure of caprolactam ion XV, which is then converted into ions XVI, XVII, and XVIII.

Fig. 2

Characteristic of compound X is also a considerable intensity of the molecular peak, which distinguishes it both from the cyclols and from cyclodepsipeptide XIX.

The conversion of the cyclols (Ia,b), stable under ordinary conditions, into cy-

Fig. 3

Figure 4: Fig. 3

Fig. 4

Figure 5: Fig. 4

clodepsipeptide forms (IIa,b) during mass spectrometry is detected (see Figs. 1, 2) by the presence in the mass spectra of peaks with m/e 99 (fragment VII), m/e 71 (fragment VIII), and m/e 70 (fragment IX), characteristic of fragmentation of the cyclodepsipeptide type.

In order to determine whether compounds (Ia,b) undergo transformations of type $B \rightleftarrows A$ under mass-spectrometric conditions, the model oxacillactam XXI was studied. However, it turned out that the latter has an entirely different fragmentation pattern (see Scheme 2).

Scheme 2

$$\underset{m/e\ 85}{\mathrm{HN}\begin{pmatrix}\text{ring}\\ \mathrm{C{=}O}\end{pmatrix}} \xleftarrow[-\mathrm{C_2H_2O_2}]{\mathrm{HOCH_2CON}} \underset{m/e\ 143}{\mathrm{XXI}} \xrightarrow[-\mathrm{CH_2O}]{} \underset{m/e\ 113}{\mathrm{HCON}\begin{pmatrix}\text{ring}\\ \mathrm{C{=}O}\end{pmatrix}} \xrightarrow[-\mathrm{H}]{} \underset{m/e\ 112}{\mathrm{O{=}C{=}N^{+}}\begin{pmatrix}\text{ring}\\ \mathrm{C{=}O}\end{pmatrix}}$$

The structure of the principal fragments formed from compounds Ia–d, X, XIX, and XXI under electron impact was confirmed by recording

Fig. 3

spectra of model compounds: butyro-, valero-, and caprolactams, their acyl and alkyl derivatives, and also caprolactone. The structures of fragments VIa,b and IX leave no doubt, since literary analogies on this question are available ([2]).

The fact of the conversion of cyclodepsipeptide X into the corresponding cyclol XI as a result of a transannular reaction proceeding under the action of

Fig. 4

electron impact is, as far as we know, the first case of the application of mass spectrometry for the detection of transannular interactions in macrocyclic systems.

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Note: Figure translations are in progress. See original paper for figures.