MASS SPECTRA AND STEREOCHEMISTRY OF SOME MACROCYCLIC PYRROLIZIDINE ALKALOIDS

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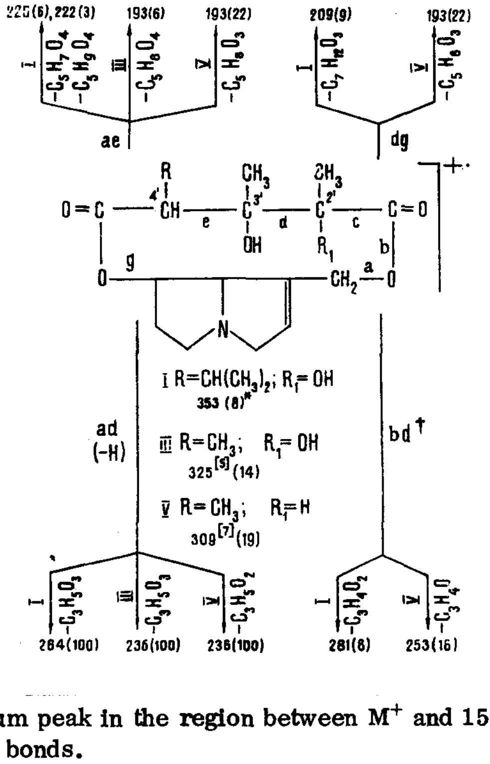
Robins and Crout [1, 2] have studied chemically the absolute configuration of the side chains of the macrocyclic pyrrolizidine alkaloids monocrotaline and trichodesmine. To prove that the alkaloids axillarine and axillaridine belong to the bases of this series, they recorded the mass spectra of nine compounds and found in them a characteristic peak (M−89 in trichodesmine) [3], which has been discussed by Spiteller [4] and Culvenor [5]. For the alkaloids crispatine [6] and fulvine [7] the relative intensities of the peaks appearing in the region of high masses have been given. The molecules of the latter two alkaloids differ only by the configuration of the OH group at C_3, but their mass spectra differ sharply. The reasons for this phenomenon are not discussed by Crout [3].

We decided to study in more detail the mass spectrum of trichodesmine (I) [8, 9] and also that of another alkaloid from the family Boraginaceae, incanine (II) [10], which has not been studied previously. We have established that in the region of low masses both alkaloids give a pattern corresponding to all bases of the retronecine type – peaks with m/e 136, 120, 119, 93, and 80 [3, 4, 11]. However, there are marked differences in the high masses. In a comparison of the spectra of (I) and (II) with the spectra given in the literature for monocrotaline (III) [4], crispatine (IV), and fulvine (V) [3], it was found that the spectra of

SCHEME 1



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* In Schemes 1 and 2, the maximum peak in the region between M^+ and 150 m/e is taken as 100%.

† Cleavages of the corresponding bonds.

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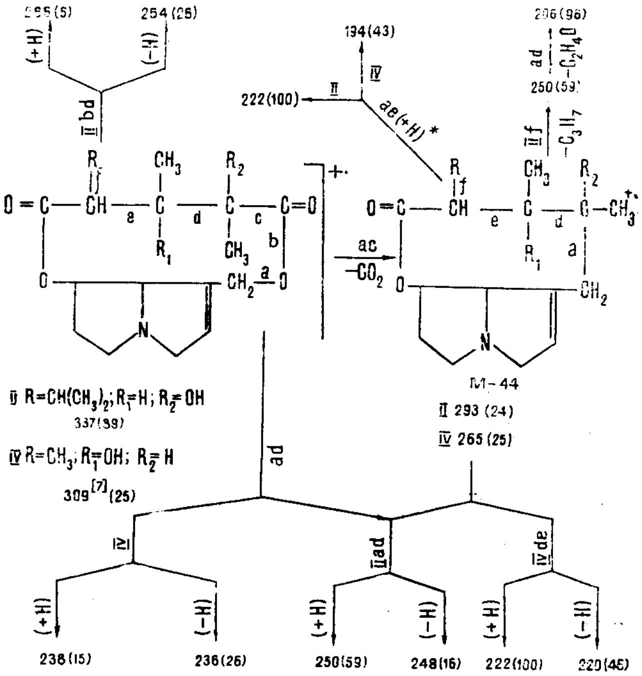
(I), (III), and (V) are practically identical, and the spectrum of (II) is similar to the spectrum of (IV). Scheme 1 shows the process of fragmentation of the ester moiety of the molecules of the first three compounds.

In addition to the molecular peak, in the region of high mass numbers there are the peaks of several fragments, the main one of which is formed by the cleavage of the *a* and d bonds with the migration of one hydrogen atom to the fragment split off. Workers who have explained this process within the framework of rearrangements of the McLafferty type [3, 4, 6] have considered that the hydrogen is split off from the hydroxy group at C_3'. To check this, we recorded the spectrum of the OD analog of trichodesime (I) and found that only ~ 20% of M^+ loses both active hydrogens in the formation of the ions M−89. Approximately 80% of these ions contain OH at C_3', while the hydrogen apparently migrates from the CH_3 group located on the same carbon atom. The ions with m/e 281 (I) and 253 (V) arise in the cleavage of bonds b and d. In the spectrum of the OD analog of (I), the peak with m/e 281 is shifted by two mass units, i.e., in this case decomposition must begin with the cleavage of bond d with transfer of hydrogen similar to that described above from the CH_3 at C_3', and the cleavage of bond b is accompanied by the migration of H· from the OH at C_2, to $-CH_2O-$.

Characteristic for all three compounds considered is the cleavage of bonds *a* and e, giving rise to ions with m/e 193 (III, V). In trichodesmine (I) the cleavage of bond e is accompanied by the migration of one hydrogen in either direction, and a pair of ions with even mass numbers (222 and 220 m/e) is formed. In the spectrum of (I), there is, in addition, a peak with m/e 209 which is shifted on deuteration by one unit and which can be obtained by the cleavage of bonds d and g. The analogous decomposition of the molecule of fulvine (V) leads to an ion with m/e 193. Thus, in the spectrum of (V) the latter ion may be composite.

SCHEME 2



The process of fragmentation of the ester moiety of the molecule of incanine (II) and of crispatine (IV) is shown in Scheme 2. The first act of decomposition is the elimination of a molecule of CO_2 (*ac*) which, as is well known, is also characteristic of alkaloids with a 12-membered ring [11, 12]. The subsequent formation of the main fragments from the M−44 ion can be explained by assuming that the ejection of CO_2 is accompanied by a contraction of the ring and not by ring closure of the side chain. In agreement with this, from the ion with m/e 265 of (IV), by de cleavage, a pair of fragments with m/e 222 and 220 arises. Ions similar in composition with m/e 250 and 248 in the spectrum of incanine (II) are obtained from the ion with m/e 293 by *a*d cleavage. Analogs of the two latter ions with respect to the position of cleavage (*a*d) in the spectrum of (IV) are the ions with m/e 238 and 236. These two pairs of ions can also be formed directly

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* (+H) indicates the migration of hydrogen to the charged fragment and (−H) to the neutral fragment.

from M^+. The ions with m/e 266 and 264 in the spectrum of (II) may be considered as pseudoanalogs of the ions with m/e 238 and 236 from (IV), since they may be a consequence of a different type of cleavage – bd – which is absent in the case of (IV).

The cleavage of bond e, which in trichodesmine and its analogs (see Scheme 1) led to the appearance of ions with a low intensity, is here the main process for the fragments with m/e 222 (100%, II) and 194 (45%, IV). Other analogs also exist in both spectra:

	M−45	M−124		
II	292(22)	213(15)	225(31)	154(15)
IV	264(46)	185(37)	225(17)	154(45)

So far as concerns the differences between the spectra of (II) and (IV), they are mainly introduced through the presence in the incanine molecule of an isopropyl group at C_1'. This leads to the formation of the ion M−43 in the spectrum of (II). An isopropyl radical can also be split off from the ion M−44, giving another variety of ions with m/e 250 (see Scheme 2), which, by losing a molecule of acetaldehyde, is converted into the intense ion with m/e 206. This form of cleavage of M^+ (II) is confirmed by the spectrum of the OD analog.

Consequently, starting from the facts that crispatine (IV) and fulvine (V) are diastereoisomers and the mass spectra of the other three compounds are similar to the spectrum of either (IV) or (V), we assumed that the alkaloids (I, III, and V) belong to the stereoisomers of one series and (II) and (IV) to the other. The necessity for this type of mass-spectrometric characterization is due to the fact that until recently there was no single opinion on the relative configuration of the OH groups in the molecule of trichodesmine (I). The ease of preparation of a cyclic sulfo ester was explained by S. Yu. Yunusov and N. V. Plekhanova [9, 13] by the presence of a cis-diol grouping. The difference in the time of oxidation of trichodesmine (I) and monocrotaline (III) by periodic acid was used by Adams [14] to show that (I) is a trans-diol and (III) a cis-diol. However, in the paper by D. Robins and D. Crout mentioned above [1], the cis orientation of the OH groups of both alkaloids was demonstrated. In addition to this, the use of such a powerful method as circular dichroism did not permit the relative positions of the substituents in the side chains of crispatine (IV) and fulvine (V) to be established [5]. On the basis of the analogies that we have found in the mass spectra, we have assumed that the hydrogen at C_2, and the hydroxyl at C_3, in the molecule of fulvine (V) have the cis orientation and in the molecule of crispatine (IV), the trans orientation. The trans position of the OH at C_2' and the hydrogen at C_3' can also be assumed for the molecule of incanine (II).

EXPERIMENTAL

The mass spectra of the samples of trichodesmine (I) with mp 160°C and of incanine (II) with mp 97°C were taken on an MKh-1303 instrument fitted with a system for the direct introduction of the sample at a temperature of the inlet tube of 110°C and an ionizing voltage of 40 V. The deuteration of (I) and (II) with deuteromethanol was performed directly in the inlet system of the mass spectrometer.

CONCLUSIONS

On the basis of the results of a comparison of the mass spectra of macrocyclic pyrrolizidine alkaloids with a known configuration of the side chain (trichodesmine, monocrotaline) with the spectra of incanine, crispatine, and fulvine a hypothesis has been put forward on the relative positions of the substituents at C_2' and C_3' in the molecules of the three latter compounds.

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