A MASS-SPECTROMETRIC STUDY OF DERIVATIVES OF THE QUINOLIZIDINE GROUP

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We have obtained and studied the mass spectra of d-epilupininic acid (I), ethyl epilupininate (II), epilupininamide (III), N,N-diethyl epilupininamide (IV), epilupinoylpiperidine (V), epilupinoylmorpholine (VI), dihydroepilusitanine (VII), piperidinoepilupinane (VIII), anhydrolupinine (IX), isoaphyllic acid (X, Fig. 1), isoaphyllamide (XI), aphylline alcohol (XII), nitrosoaphylline alcohol (XIII, Fig. 2), aphyllic acid (XIV), nitrosoaphyllic acid (XV), aphyllamide (XVI), methyl aphyllate (XVII), ethyl nitrosoaphyllate (XVIII), and ethyl N-benzoylaphyllate (XIX) [1, 2].

The mass spectra were taken on an MKh-1303 mass spectrometer with the direct introduction of the substance into the ion source at an ionizing voltage of 40 V and a temperature of 100-150°C. We obtained epilupininic acid (I), with mp 255°C both from lupinine and from epilupinine. On comparison, the two products proved to be identical [2].

Substances (I-XI) are derivatives of trans-quinolizidine and (XII-XIX) are derivatives of cis-quinolizidine. Of the derivatives of trans-quinolizidine, the mass spectra of lupinine, epilupinine, and lupininic acid have been studied previously [3]. The mass spectra of derivatives of cis-quinolizidine have not been studied previously. The results of the mass spectroscopy of groups of alkalides, mainly sparteine and matrine, belonging to more complex cyclic systems containing trans and cis linkages are discussed in a number of publications [4, 5].

The main characteristics of the mass spectra of trans-quinolizidine derivatives with a 1-equatorial side group (I-VIII) and 1-equatorial-3-axial side groups of atoms (X and XI) are given in Table 1.

The results of a comparison of these spectra show that the main direction of the fragmentation of compounds (I-VIII), as also of epilupinine [3], is the ejection of the equatorial substituent and β decompo-

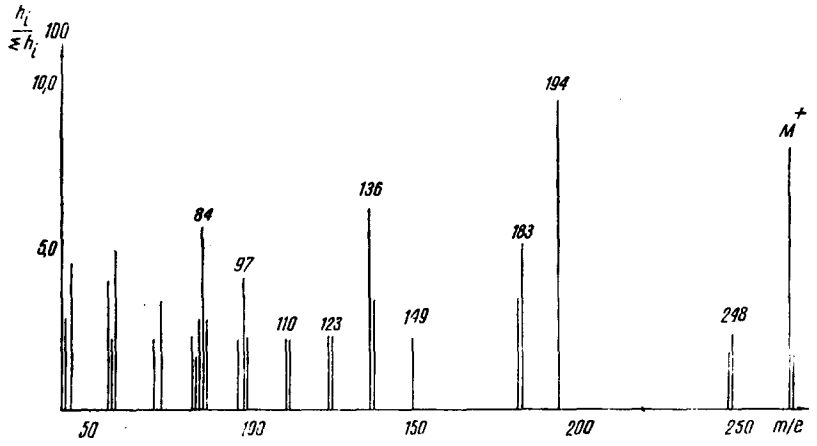

Fig. 1. Mass spectrum of isoaphyllic acid.

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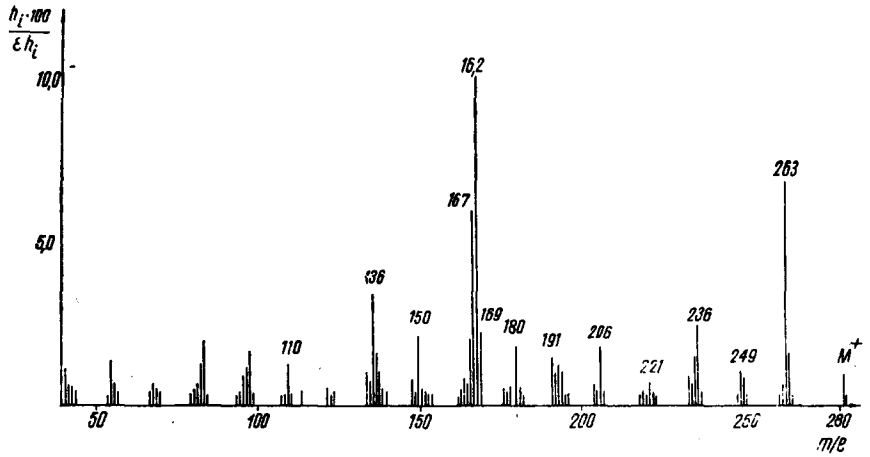


Fig. 2. Mass spectrum of nitrosoaphylline alcohol.

TABLE 1

Peaks of the ions, m/e	Relative intensity, %									
	I	II	III	IV	V	VI	VII	VIII	IX	X
152	—	—	—	—	—	—	4,3	6,9	—	—
151	—	—	—	—	—	—	7,6	19,6	—	2,0
150	—	—	—	—	—	—	3,1	2,2	—	—
149	—	—	0,8	—	—	0,3	0,4	0,4	2,2	2,0
138	2,3	4,8	4,5	10,0	11,0	6,0	7,7	1,9	—	1,2
136	3,6	1,4	3,0	3,5	4,0	2,7	5,2	5,9	6,2	1,6
124	1,8	2,4	2,3	2,3	2,2	2,3	1,5	1,5	2,2	1,6
123	2,1	2,5	4,3	2,9	2,4	2,5	1,4	1,0	2,2	1,2
111	3,9	6,2	7,1	5,7	5,9	5,3	4,0	0,6	2,2	2,0
110	2,9	5,1	5,9	4,9	4,4	3,8	4,1	1,3	2,2	2,0
98	3,6	1,7	1,9	2,0	1,8	1,9	1,8	20,0	2,2	1,6
97	4,6	7,1	5,2	6,0	5,0	3,7	3,4	1,7	4,0	3,2
84	2,9	1,6	1,6	1,2	4,7	1,2	1,8	2,0	5,5	5,7
83	5,4	10,6	10,6	5,4	2,5	4,8	2,8	1,6	2,8	2,4
58	11,5	—	—	0,5	0,5	0,4	0,8	—	—	—
55	5,1	5,3	5,1	4,0	0,6	2,7	2,8	3,3	4,0	2,4
41	4,6	2,1	2,4	1,4	2,3	1,1	0,1	4,0	2,8	1,6

sition with respect to the 1–10 bond. Because of this, the mass spectra lack ions with m/e 139, 125, 57, and 45, the formation of which is associated with the migration of hydrogen to the positively charged part of the molecule on its breakup. Intense peaks of the molecular ions are characteristic of these compounds.

The β decomposition of d-epilupininic acid (I) gives peaks of ions with m/e 111, 97, and 83; decarboxylation ions with m/e 136, 137, and 138 can arise directly from a molecular ion. The positive charge may also be localized on the carboxy group, and in this case the maximum peak is that of an ion with m/e 58 – $[C_2H_2O_2]^+$.

Because of the decomposition of the ethoxycarbonyl group, ethyl epilupininate (II) forms ions with m/e 182 ($M-C_2H_5$; 8.0%) and 166 ($M-OC_2H_5$; 3.9%), in addition to the ions (I).

The breakdown of the side chain of epilupininamide (III) forms ions with m/e 165 (0.6%) and 164 (1.3%). The ejection of 29 amu and the formation of an ion with m/e 153 (0.8%) is possible in the case of β' decomposition with respect to the basic nitrogen atom.

N,N-Diethylepilupininamide (IV) gives the maximum peak of an ion with m/e 138. Decomposition at the diethylamide group gives ions with m/e 209 ($M-C_2H_5$; 0.9%), 166 (1.3%), and 164 (0.6%).

In the case of epilupinoylpiperidine (V), the maximum peak is again that of the ion with m/e 138. On decomposition at the lactam group, an ion with m/e 208 arises. The fact that the peak of the ion with m/e 84 is stronger than that of the ion with m/e 83 is due to the formation of a peak from the piperidine residue of the side group.

In addition to the usual ions, epilupinoylmorpholine (VI) gives ions with m/e 164 (0.6%), 166 (1.0%), and 210 (0.7%). The latter corresponds to the ion with m/e 208 arising from (V). The decomposition of the morpholine ring leads to an ion with m/e 222 ($M-CH_2O$; 0.9%).

TABLE 2

Ions	Relative intensity, %							
	XII	XIII	XIV	XV	XVI	XVII	XVIII	XIX
M	5,5	1,0	0,3	0,5	1,3	2,2	0,7	7,1
M−1	0,5	—	—	—	—	—	—	8,7
Φ_1	3,8	16,2	—	12,7	2,6	3,1	9,5	11,5
Φ_2	1,3	0,9	—	2,4	6,7	2,7	0,5	4,3
M−72	8,1	—	—	3,2	2,0	4,0	—	—
150	1,1	2,1	0,6	0,9	0,3	—	0,5	—
149	0,9	0,4	1,2	1,0	0,5	0,5	0,3	—
136	1,8	3,4	5,1	1,8	3,0	2,5	5,3	7,1
124	1,3	0,4	1,1	0,4	1,5	3,0	1,1	3,8
123	0,7	0,3	1,4	0,5	1,3	0,9	0,8	0,9
122	0,8	0,5	0,8	0,4	0,7	1,1	1,1	1,7
110	2,6	1,2	1,6	0,8	2,3	3,8	2,0	3,2
98	3,4	1,6	1,4	0,6	2,5	5,5	1,5	0,8
97	2,7	1,2	2,4	0,9	2,9	5,7	2,0	1,3
84	12,5	2,9	1,6	1,3	2,9	11,0	7,7	0,9
83	1,6	1,2	2,0	0,9	2,4	2,7	3,4	—
69	1,2	0,5	1,9	0,5	2,1	1,4	1,0	—
68	0,9	0,6	0,6	0,2	1,5	2,2	0,8	—

The probabilities of β decomposition with respect to each of the two nitrogen atoms in piperidino-epilupinane (VIII) are approximately the same. In the spectrum of this compound, the peaks of ions with m/e 151 and 98 have the same intensity.

In order to check W. Grow's hypothesis [6], we recorded the mass spectra of lupinine, epilupinine, and lupinine methiodide. The mass spectrum of lupinine methiodide contains all the peaks of epilupinine, of iodine, and of methyl iodide. A comparison of the mass spectra confirms the equatorial position of the hydroxymethyl group in lupinine methiodide.

On mass-spectrometric decomposition, the double bond in anhydrolupinine (IX) leads to the formation of the most stable ion $[M-1]^+$. In this ion, the positive charge is stabilized as a result of the conjugation of the double bonds. The fragmentation of (IX) differs from that of the compounds considered by β decomposition with respect to ring A, which leads to the appearance of ions with m/e 136 (12.6%) and 122 (4.0%).

The α-piperidine residue in position 3 of quinolizidine in isoaphyllic acid (X) changes the nature of the mass-spectrometric decomposition: the strongest ion is that with m/e 194 formed by double β and β' decomposition with respect to the two nitrogen atoms, while the quinolizidine ring undergoes β' decomposition. Isoaphyllic acid does not give an M−44 ion (see Fig. 1). Ions corresponding to decarboxylation − m/e 136 (6.2%) and 137 (3.4%) − arise from intermediate ions with m/e 182 (3.4%) and 183 (5.0%). The formation of an ion with m/e 183 (M−83), which is possible only with the migration of the β-hydrogen or the hydrogen on the nitrogen atom of the piperidine residue to the positively charged part of the molecule, confirms the equatorial position of the piperidine residue in the initial molecule.

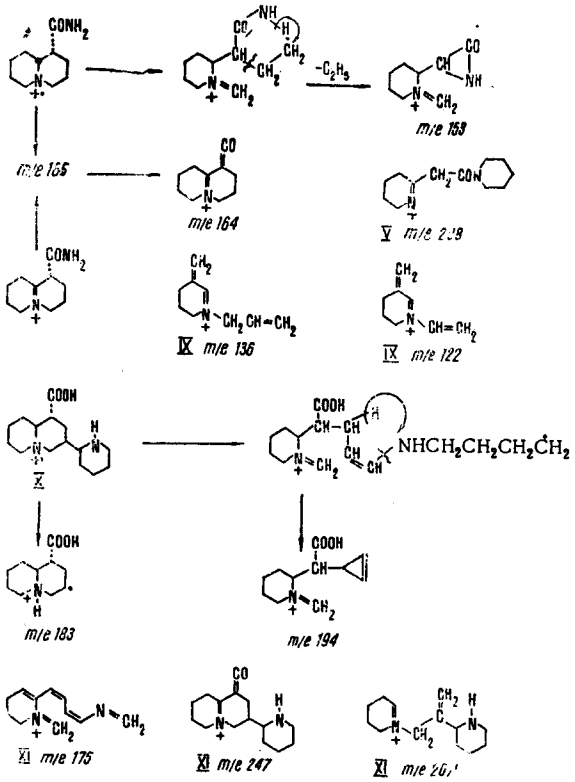
When the positive charge is localized on the piperidine residue, an ion with m/e 84 (5.5%) is formed.

Some ions of isoaphyllamide are analogous to those given and are shifted by one mass unit: m/e 193 (6.1%), 182 (3.2%), and 181 (2.8%). An ion with m/e 84 (5.7%) is also formed. In addition to an ion with m/e 193, and ion with m/e 175 arises in which stabilization takes place as a result of the formation of conjugated double bonds. The decomposition of the amide group leads to the formation from the molecular ion of ions with m/e 249 ($M-NH_2$), 221 ($M-CONH_2$), and 207. Analogous ions are formed in the decomposition of the ion $[M-1]^+$: m/e 248 and 219. The ions with m/e 249, 248, and 247 are converted by the ejection of the piperidine residue into ions with m/e 165, 164, and 163.

For all the compounds considered above, which are trans-quinolizidine derivatives, the most characteristic ions are those with m/e 111, 123, and 138 (see Table 1).

The basic results on the mass spectra of the cis-quinolizidine derivatives (XII-XIX) are given in Table 2. Only two or three intense peaks are characteristic for these compounds, the formation of these peaks being connected with the ejection of a piperidine or substituted piperidine residue (Φ_1). The other ions are usually of low intensity. From them we may single out the fragment appearing on the ejection of the 1-equatorial substituent (Φ_2) and the $[M-72]^+$ ions. The molecular ions are usually unstable and are

therefore of low intensity. The $[M-1]^+$ ions do not appear, either. Of the common ions, those characteristic for cis-quinolizidine derivatives have m/e 68 or 69, 97 or 98, 149 or 150, and 136. In the spectra of these compounds, the ion with m/e 138 is absent or has a very low intensity. The compounds studied form ions as a result of the decomposition of the functional groups. Aphyllic acid (XIV) undergoes cyclization to α-isoaphylline under the conditions of mass spectrometry. Consequently, with the exception of the peak of the corresponding molecular ion, in this case the spectrum of α-isoaphylline is repeated.



We have recorded the mass spectrum of α-isoaphylline (mp 105-106°C). This spectrum proved to be different from that published by Schumann et al. [4] and identical with the spectrum of aphylline described in the same paper. The latter spectrum is unlike the mass spectrum of aphylline recorded by us. The main features of the spectra that we obtained are: for α-isoaphylline m/e 248 (8.5%), 247 (5.6%), 220 (5.0%), 149 (1.2%), 138 (2.6%), 137 (4.3%), 136 7.8%); for aphylline m/e 248 (1.3%), 247 (1.0%), 220 (0.8%), 149 (0.8%), 150 (1.1%), 151 (1.9%), 152 (3.0%), 153 (5.1%), 138 (7.5%), 137 (1.5%), 136 (2.7%). In the case of isoaphylline, the molecular ion decomposes exclusively at the ring with the lactam nitrogen function, and in the case of aphylline mainly at this ring.

SUMMARY

The results of a mass-spectrometric study of 1- and 1,3-substituted derivatives of cis- and trans-quinolizidines are given. The compound investigated formed, in addition to the common ions with m/e 124, 110, 97, 54, and 41, ions specific for the trans- and cis-linkage of the rings and ions characteristic of the side chains occupying equatorial or axial positions. In addition, the mass spectra of the cis-quinolizidine derivatives are characterized by a small number of strong peaks and by a low intensity of the molecular ions.

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