MASS SPECTRA OF PYRROLIZIDINE ALKALOIDS OF THE HELIOTRIDANE SERIES

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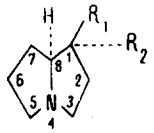
UDC 543.51+547.944/945

Information on the mass spectrometry of the pyrrolizidine alkaloids has been published previously [1-5]. However, there is no information on the fragmentation of bases of the heliotridane series, with the exception of the amino alcohol laburnine [1].

Compounds of the heliotridane group possess a saturated pyrrolizidine skeleton. In view of this, substituents at C_1 may occupy either the cis or the trans position with respect to the 8-H. The alkaloids that we have studied are based on two stereoisomeric amino alcohols: trachelanthamidine (I) and lindelofidine (II) [(+)-isoretronecanol].



I $R_1 = H$; $R_2 = CH_2OH$

II $R_1 = CH_2OH$; $R_2 = H$

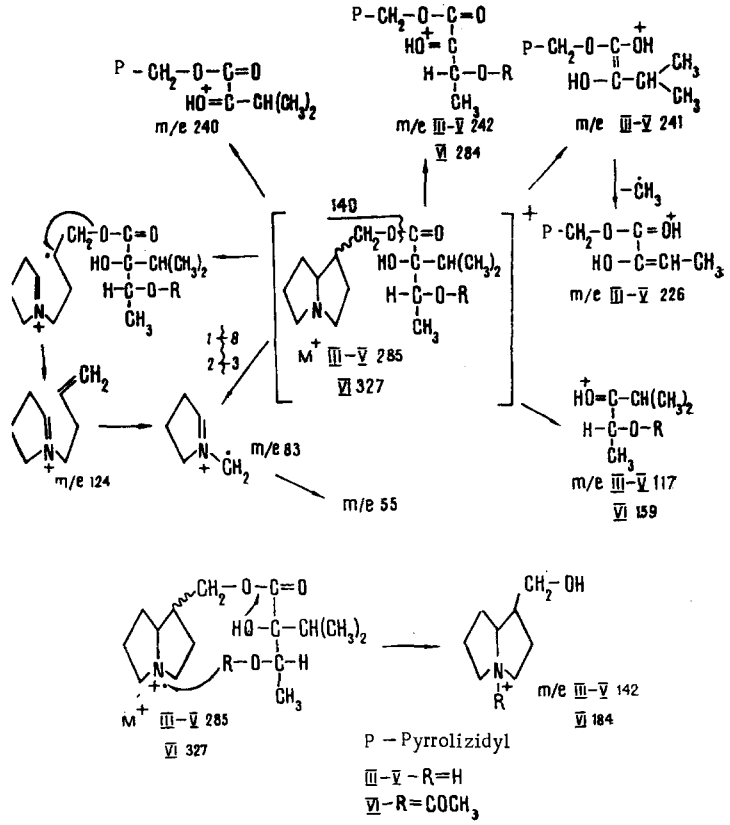
The amino alcohol (I) forms with viridifloric acid the ester viridiflorine (III) [6], and with trachelanthic acid, trachelanthamine (IV) [7]. The latter acid, in combination with the amino alcohol (II), gives the alkaloid lindelofine (V) [6]. The two acids mentioned are distinguished by the relative positions of their hydroxy groups.

As was to be expected, the mass spectra of viridiflorine (III) and trachelanthamine (IV) are very similar. Small differences in the intensities of the fragmentary ions are observed only in the region of high masses (Fig. 1). The molecular ions appear in the form of peaks of low intensity. The M−1 ions, formed mainly by the detachment of the hydrogen atom from C_8, are of equal intensity to them. A certain number of ions of this type may arise by the splitting off of H· from the OH group, since in the calculation of the molar contents in the spectra of the OD analogs (according to Biemann [8]), small residues were obtained. The presence of a bulky branched and oxygen-rich substituent creates the prerequisites for the localization of the charge in the side chain. For this reason, a number of fragments are formed in the high-mass region. The alternative and alternate splitting off of methyl groups and a molecule of water leads to the appearance of M−15, M−18, and M−33 ions. The shift of the M−33 ion by one mass unit in the spectrum of the OD analogs shows that the water molecules are ejected in the form of HDO. Triplets in the 240-242 m/e region arising through the localization of the charges on the oxygens of the tertiary hydroxy groups are of considerable intensity in the spectra of (III) and (IV). Ions with m/e 242 are products of the splitting out of an isopropyl group from M^+ (see scheme). The fragments with m/e 240 are formed by the splitting out of secondary ethanol radicals. The ejection of molecules of acetaldehyde (ions with m/e 241) takes place through six-membered transition states with the migration of the hydrogen of the secondary OH group to the ester oxygen atoms. The ions with m/e 241, losing methyl radicals, are stabilized in the oxonium form (m/e 226). The structures of the fragments mentioned are confirmed by the corresponding shifts of the peaks in the spectra of the OD analogs of (III) and (IV) (see Fig. 1).

The peaks of greatest intensity in the spectra of the alkaloids considered generally appear in the field of low mass numbers. They are formed by the elimination of the acyl or acid residue with the localization of the charge on the nitrogen atom. The maximum ion with m/e 124 is obtained by the cleavage of the C_1-C_8

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 634-639, September-October, 1972. Original article submitted February 21, 1972.

and CH_2-O bonds. The ejection of a propenyl radical from the latter leads to the formation of the ion with m/e 83, which is the most characteristic ion for pyrrolizidines [1]. This ion, in its turn, may arise directly from M^+. One of the forms of the ion with m/e 83, by losing a molecule of ethylene, is converted into an ion with m/e 55 [1, 3, 5]. A satellite of the ion with m/e 83 is an ion with m/e 82 which is also known for the pyrrolizidines [1, 3, 5] (see scheme).



The greatest interest is aroused by the second-most intense ion with m/e 142. In the spectra of the OD analogs, this peak has shifted by two mass units in the same ratios as the molecular peak. The mass number, measured on a high-resolution instrument is 142.1241, which corresponds to the composition $C_8H_{16}ON$ (accurate value 142.1231 at c = 12,000,000). Thus, the ion under consideration is the protonated form of the amino alcohol formed on the splitting off of the acid residue with the simultaneous migration of two alcoholic hydrogens into the charged fragment. In addition to this, the spectra show small proportions of ions with m/e 140 apparently obtained by the heterolytic cleavage of the O – CO bond.

To confirm the course of fragmentation described above, the mass spectra of a number of derivatives were recorded. In the spectra of the monoacetate of trachelanthamine (VI), in the region of low mass numbers the pattern was basically similar to that of the alkaloids (III) and (IV). In addition to this, two new peaks appeared in this region. An ion with m/e 184 (142 + 42) shows the possibility of the migration of the acetyl radical to the nitrogen atom and may be the acetyl analog of the ion with m/e 142. In this case, the latter may be formed from the ion with m/e 184 by the ejection of a ketone molecule. The mass number of the ion with m/e 184 is 184.1335 ($C_{10}H_{18}O_2N$ = 184.1338). The ion with m/e 159 is obtained with the localization of the charge on the oxygen of the tertiary OH group as a result of the splitting off of the ester residue together with the pyrrolizidine nucleus. The small peak of ions with m/e 117 present in the spectra of the initial alkaloids (shifted by two units in the spectra of the OD analogs) consequently represents the deacyl analog of this ion.

In the region of high mass numbers of the spectra of the monoacetate (VI), the ion with m/e 240, of the same composition as in (III) and (IV), has the greatest intensity. The formation of the ion with m/e 241 takes place this time with the migration of the hydrogen from the CH_3 group (McLafferty decomposition) [1] with the ejection of a molecule of vinyl acetate. In addition, in the spectrum of (VI) there is a low-intensity peak of an M – 44 ion (with m/e 283), the appearance of which may be connected with the ejection of a molecule of acetaldehyde with the simultaneous migration of the acetyl radical to the quaternary carbon atom. The peaks with m/e 242 in the spectra of (III) and (IV) are shifted to m/e 284 in the spectrum of (VI).

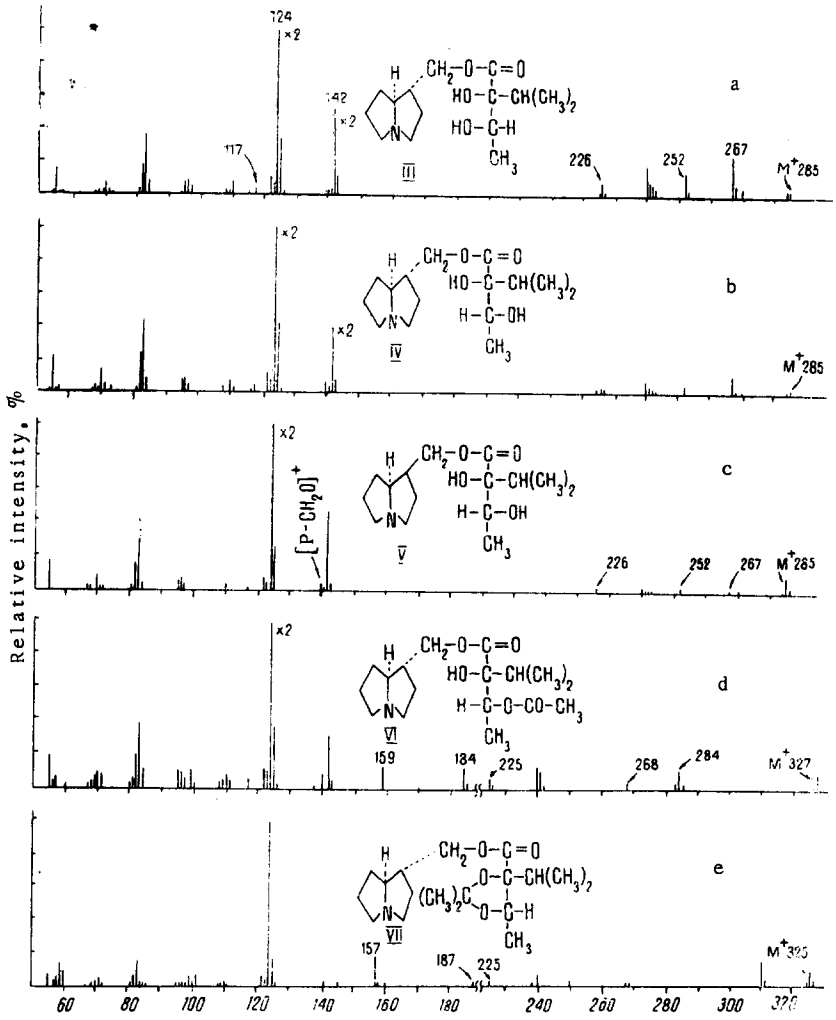


Fig. 1. Mass spectra of viridiflorine (a), trachelanthamine (b), lindelofine (c), trachelanthamine acetate (d), and viridiflorine acetonide (2).

A maximum peak with m/e 124 is characteristic for viridiflorine acetonide (VII). No ion with m/e 142 is formed, and the ion with m/e 140 has a very low intensity. A number of considerable peaks arise as the result of the fragmentation of the acetonide group (M−15, M−58, M−75, and 59). The most prominent of this series is the peak with m/e 157 formed by the ejection of the ester moiety of the molecule from M^+ of the acetonide (VII).

Let us now consider the spectrum of the alkaloid lindelofine (V) (see Fig. 1). It contains the same peaks as the spectra of (III) and (IV). However, the ratios of the intensities of the peaks have changed substantially. In order to compare them, we give the contributions of the main ions of the spectra of viridiflorine and lindelofine to the total ion current.

Substance	55	82	83	96	124	140	142	226
III	1,60	2,08	4,08	0,96	21,90	0,83	11,50	0,71
V	3,54	3,32	8,35	1,60	38,20	1,07	9,32	0,21

Substance	240	241	242	252	267	270	284	M^+285
III	2,08	0,88	0,84	1,46	2,50	0,42	0,29	0,25
V	0,54	0,32	0,21	0,64	0,21	0,11	0,32	2,05

The most fundamental feature of the spectrum of lindelofine (V) is the increase in the stability of the molecular ion which, in this case, is approximately eight times more intense than in viridiflorine (III), this obviously being connected with a change in the orientation of the substituent at C_1. In addition to the increase in the intensity of M^+ there is a decrease in the contribution of fragments formed by the localization of the charge in the side chain. If the above contributions of the ions are summed, beginning with the ion of 226 m/e and going up to M^+, inclusive, the sum for viridiflorine will be approximately twice as great as for lindelofine. For ions localizing the charge on the nitrogen atom (from 55 to 142 m/e), conversely, their fraction of the total ion current in lindelofine is far greater than in viridiflorine.

The intensities of the M−1 peaks in the spectra considered are apparently similar. However, on calculating the molar proportions in the group of M^+ peaks in the spectrum of [D] lindelofine more residues are obtained than in viridiflorine, which shows a relatively greater participation of OH groups in the formation of the M−1 ions. The splitting off of hydrogen from C_8 in viridflorine may be affected by the steric influence of the cis substituent with respect to it at C_1. In the molecule of lindelofine (H_8/R_1 trans) this influence is apparently not so great.

We have also compared the mass spectra of the amino alcohols trachelanthamine (I) and lindelofidine (II). The values given below of the relative intensities of the main peaks of these spectra differ only slightly.

Substance	141 (M^+)	140	124	110	83	82	55
I	23,8	9,1	15,2	9,1	100,0	37,0	21,2
II	24,0	10,0	16,6	10,5	100,0	50,0	25,5

Thus, the standard use of the method of electron impact does not permit pyrrolizidine amino alcohols with different orientations at C_1 to be distinguished. If a large substituent is present, it does become possible to distinguish the isomers. This hypothesis requires further confirmation.

EXPERIMENTAL

The mass spectra were taken on an MKh-1303 instrument with a system for the direct introduction of the substance at 80-100° C with an ionizing voltage of 40 eV. The OD analogs were obtained by immersing the samples for a short time in CD_3OD. The elementary composition of the 142 ion in the spectrum of (III) was determined on an MS-902 instrument by M. I. Gorfinkel (Novosibirsk).

Trachelanthamidine (I). The substance was obtained by the hydrolysis of (IV) [9]; bp 134° C at 8 mm Hg, n_D^{20} 1.4980.

Lindelofidine (II) was synthesized by the saponification of (V) [10]; bp 108° C at 3 mm Hg, mp 42° C.

Viridiflorine (III), mp 102.5-103.5° C; Trachelanthamine (IV), mp 91-92° C; and Lindelofine (V), mp 106-107° C. These alkaloids had been isolated at various times by workers of the laboratory of alkaloid chemistry of the Institute of the Chemistry of Plant Substances of the Academy of Sciences of the Uzbek SSR.

Trachelanthamine Acetate (VI). To 3 g of trachelanthamine (IV) was added 5 g of acetic anhydride (the mixture became hot and the substance (IV) dissolved), after 12 h 10 ml of water was added, and the mixture was neutralized with potassium carbonate and extracted three times with chloroform, after which the chloroform extract was dried with potassium carbonate. Evaporation of the solvent and chromatography of the residue on a column of Al_2O_3 (solvent chloroform−methanol) gave a product with mp 75° C (from acetone).

Viridiflorine Acetonide (VIII). To a solution of 500 mg of viridiflorine in 20 ml of absolute acetone was added 1 g of conc. H_2SO_4, and the mixture was left for 12 h; it was then neutralized with anhydrous potassium carbonate and filtered from inorganic material. The filtrate was evaporated to dryness, giving 500 mg of the liquid acetonide.

SUMMARY

The fragmentation in the mass spectra of three pyrrolizidine alkaloids and two amino alcohols has been studied. The spectra of alkaloids with different orientations of the substituent at C_1 differ appreciably from one another in the ratio of the intensities of the fragments.

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