MASS SPECTRA OF PYRROLIZIDINE ALKALOIDS

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The majority of pyrrolizidine alkaloids isolated from plants are esters of hydroxy derivatives of 1-methylpyrrolizidine (necine alcohols). The esterification of the alcohols with acids containing chains of five to seven carbon atoms at C_9 or at C_9 and C_7 forms monoester and diester bases. The combination of dibasic acids (C_{10}) with the amino dihydroxy alcohols gives the group of macrocyclic pyrrolizidine alkaloids.

In agreement with the structure of the pyrrolizidine bases, their mass spectra show two regions enriched with peaks. The first group of fragments is formed as the result of the elimination from M^+ of individual elements of the side chains. The second group consists of a main fragment arising chiefly by the splitting out of the acyloxy radical and of the products of the subsequent decomposition of the amino alcohol. In view of this, analysis of the mass spectra of the pyrrolizidine alkaloids consists in determining the nature of the amino alcohol in the region of low mass numbers and determining the structure of the side chains from the peaks located close to the molecular ion (between M^+ and the main fragment).

The bulk of the information on the mass spectra of the group of bases considered is contained in reports of work on the proof of the structure of particular natural samples. A paper by Spiteller's group, which gives the characteristics of the mass spectra of the main types of amino alcohols and also of monoester and macrocyclic alkaloids approaches most closely to the definition of a review. A later publication by Danish workers [2] making use of isotopic substitution and the measurement of elementary composition and ion appearance potentials contains important information.

The aim of the present review was to generalize information on the mass spectrometry of the pyrrolizidine alkaloids and to compare the properties of the various subgroups of these compounds. Some emphasis has been placed on the reflection of the isomerism of the molecules in the spectra and on details of the decomposition of the side chains and of macromolecules connected with this question.

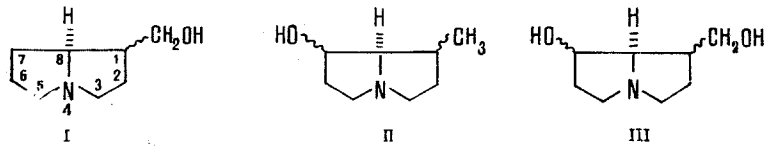
Fragmentation of the Necine Alcohols

All the alcohols are divided into three main groups: the heliotridane, heliotridine, and otonecine groups.

The mass spectrum of the only representative of the third group, otonecine (VI) has not been studied.

Heliotridane Group. The decomposition of the molecular ions of the amino alcohols of this type begins with the cleavage of the C_1-C_8 or the C_7-C_8 bond. The contribution of each process depends on the presence of hydroxy groups at C_7 and C_9.

Heliotridane Group



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Institute of the Chemistry of Plant Substances, Academy of Science of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 153-170, March-April, 1978. Original article submitted October 16, 1977.

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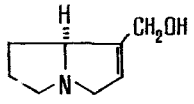
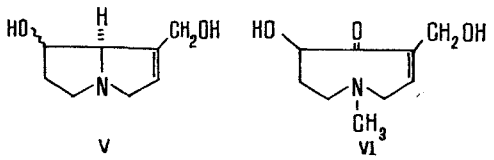
Heliotridine Group



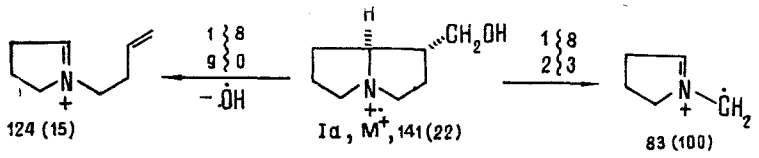
IV

Otonecine Group



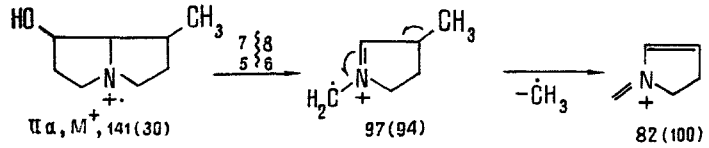
V VI

In the spectrum of laburnine [1, 3] (Ia) (α-CH_2OH), the peaks of ions formed as the result of C_1-C_8 cleavage predominate (Scheme 1).



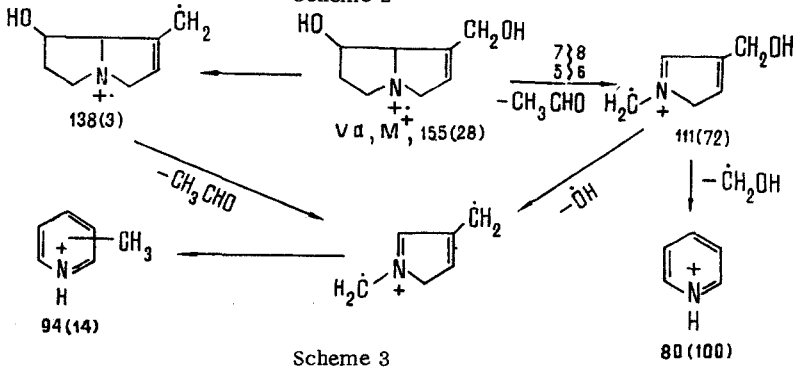
124 (15) Ia, M^+, 141 (22) 83 (100)

Scheme 1



IIa, M^+, 141 (30) 97 (94) 82 (100)

Scheme 2



138 (3) Va, M^+, 155 (28) 111 (72) 94 (14) 80 (100)

Scheme 3

On comparing the spectra of the optical antipode of laburnine — trachelanthamidine (Ib) [4] — and lindelofidine (Ic) (β-CH_2OH) only small differences are observed in the relative intensities of the main fragments [5]:

m/e	*I* b	*I* c
141 M^+	24	24
140	9	10
124	15	17
110	9	10
83	100	100
82	37	50
55	21	25

The molecular ion of retronecanol (IIa) (7β-OH) [6] decomposes mainly through the stage of C_7-C_8 cleavage [1] (Scheme 2). A similar spectra is observed for the isomeric 7α-hydroxyheliotridane (IIb) [7, 8].

A feature of the mass spectra of platynecine (III) [1] and its stereoisomers [9, 10] is the pronounced decrease in the stability of M^+ and the hydroxy analog of the ion with m/e 97 (m/e 113):

$$157\,(M^+,\ 8)\xrightarrow{5\,\}\,6}113\ (20)\xrightarrow[-\,\dot{C}H_2OH]{}82\ (100).$$

The characteristic directions of fragmentation of amino alcohols with the heliotridane skeleton shown above have been used by some workers to establish the structures of the new necine alcohols macronecine [10], croalbinecine [11], and 1α-methoxymethyl-1β,2β-epoxy-8α-pyrrolizidine [12] and its analogs [13].

Heliotridine Group. The directions of fragmentation of supinidine (IV) [14], retronecine (Va) (7β-OH) [1], and heliotridine (Vb) (7α-OH) [2] are analogous to those of the amino alcohols of the heliotridane group with the difference that because of the presence of the $C_1=C_2$ π bond the alternative elimination of the hydroxy radical from C_9 and of the C_7-C_8 chain appears more distinctly, leading to an ion with m/e 94 (Scheme 3).

The increased probability of the splitting out of $\dot{C}H_2OH$ from the ions with m/e 111 is explained by the stabilization of the ion with m/e 80 in the form of the pyridinium cation [1].

Pedersen and Larsen [2] have found that the difference in the ionization potentials of retronecine (Va) and heliotridine (Vb) and of the appearance potentials of the ions with m/e 111 and 80 are within the limits of the error of measurement for these isomers.

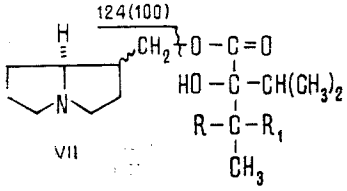
Thus, the following peaks are characteristic for the amino alcohols (I-V):

I.	141 (M^+),	124, 83 (100)
II.	141 (M^+),	97, 82 (100)
III.	157 (M^+),	113, 82 (100)
IV.	139 (M^+),	94, 80 (100)
V.	155 (M^+),	94, 80 (100)

Fragmentation of Ester Alkaloids with the Heliotridane Skeleton

Mass spectrometry has played an important role in the determination of the structure of a number of alkaloids isolated from plants of the family Orchidaceae. They are based on the nucleus of laburnine or its isomers esterified with acetic acid [15], the methyl ether of 2-benzylmalonic acid [16, 17], and 2-isobutylmalonic acid [18]. The authors mention that in the spectra of all the alkaloids isolated, including hammarbine [19] with a molecular weight of 502 the maximum peak is that of an ion with m/e 124 which, in combination with the intense peak of a fragment with m/e 83, characterizes the pyrrolidine skeleton.

Alkaloids with the heliotridane nucleus are characteristic of Central Asian plants of the family Boraginaceae [20]. In a previous paper [5] we have compared the spectra of three isomers: viridiflorine (VIIa), trachelanthamine (VIIb), and lindelofine (VIIc). The relative intensities of the fragments in the spectra of (VIIa) and (VIIb) differ little from one another.



VII

VIIa: α-CH_2O—; R=OH; R_1=H
VIIb: α-CH_2O—; R=H; R_1=OH
VIIc: β-CH_2O—; R=H; R_1=OH

When (VIIa) and (VIIc) are compared with one another, however, substantial quantitative differences can be seen in the contributions of the main ions to the total ion current:

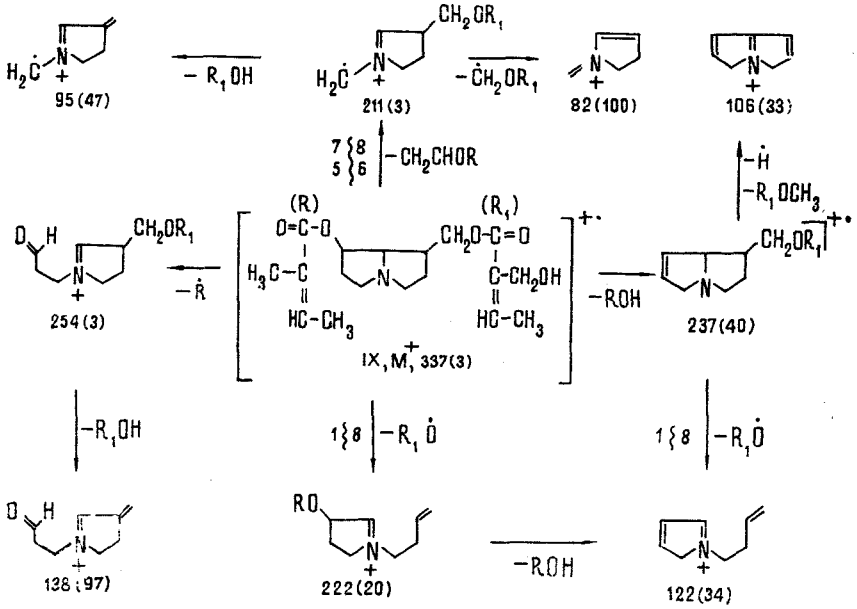
m/e	*VII*a	*VII*b
55	1,60	3,54
83	4,08	8,35
124	21,9	38,2
142	11,5	9,32
226 ($M-C_2H_4O-CH_3$)	0,71	0,21
240 ($M-C_2H_5O$)	2,08	0,54
241 ($M-C_2H_4O$)	0,88	0,32
242 ($M-C_3H_7$)	0,84	0,21
252 ($M-H_2O-CH_3$)	1,46	0,64
267 ($M-H_2O$)	2,50	0,21
285 (M^+)	0,25	2.08

These differences may serve as a basis for the recognition of monoester alkaloids with the trachelanthamidine nucleus (Ib) and the lindelofidine nucleus (Ic). The redistribution of the intensities of the main ions in favor of the peak of the ion with m/e 124 in the spectrum of the alkaloids is explained by the stability of the neutral fragment slit off in the formation of this ion.

The main feature of the fragmentation of (VIIa-c) is the formation of the ion of a protonated amino alcohol with m/e 142 ($C_8H_{16}ON$). Deuteration of the alkaloids has shown [5] that in the main process the hydrogen atoms of both OH groups migrate to the pyrrolizidine nucleus. The spectrum of trachelanthamine acetate (VIII) contains the acetylated form of the ion with m/e 142 (m/e 184) while in the spectrum of the acetonide of viridiflorine there are no ions of this type.

The spectra of viridifloric and of heliotric acids and their methyl esters have been considered [21]. The main directions of decomposition of these compounds pass through the diol cleavage of a C — C bond.

Let us consider the fragmentation of bases with the platynecine skeleton for the case of the diester alkaloid sarracine (IX) as example [22, 23]. Numerous methods of splitting off the two substitutents at C_7 and C_9, of approximately equal volume, leads to the appearance of a large number of intense peaks in the spectrum of sarracine (IX). Stabilization of the fragments takes place as the result of the competing C_1-C_8 and C_7-C_8 cleavages followed by the elimination of the acyl or acyloxy radicals and also by the elimination of RCOOH and R_1COOH molecules (Scheme 4).



Scheme 4

Fragmentation of the Ester Alkaloids with the Heliotridine Skeleton

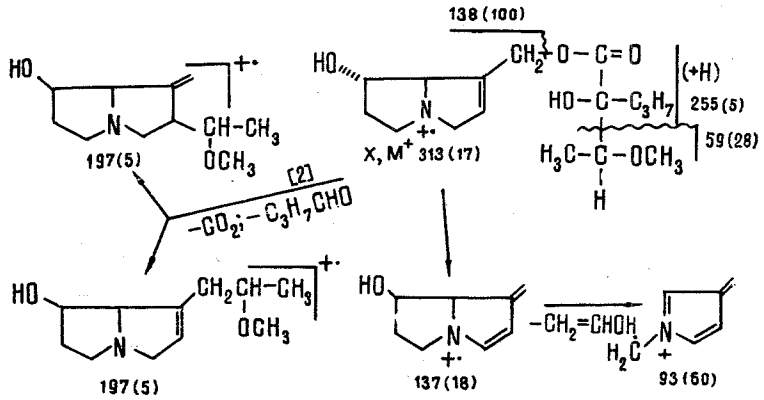
Monoester Alkaloids. In the case of heliotrine (X) as example, it has been established [1] that alkaloids with the heliotridine skeleton (V) form an allyl cation with m/e 138 as the 100% ion. The fragment next in intensity with m/e 93 arises through the stage of an ion with m/e 137.

The ions with m/e 94 and 80 that are characteristic for amino alcohol (V) are of only second-degree importance in the spectrum of heliotrine. Of the products of the decomposition of the side chain, Spiteller et al. [1] mention an ion with m/e 255 arising as the result of the splitting out from M^+ of a methyl vinyl ether molecule. This fragment is analogous to the ions with m/e 241 in the spectra of the heliotridane bases (VII).

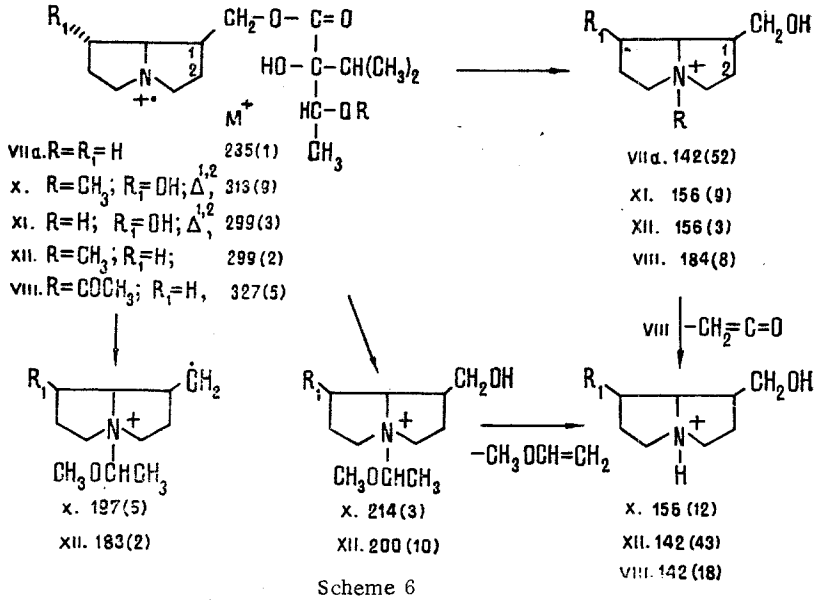
The decomposition of the side chain by the same C—C bond forms the basis of two unusual processes reported by Pedersen and Larsen [2] for the spectrum of heliotrine (X). The first consists in the synchronous elimination from M^+ of CO_2 and butyraldehyde molecules and the migration of the $CH_3\dot{C}HOCH_3$ radical from C_2 to C_9 (Scheme 5). The mechanism of the second process is not given, but on the basis of a measurement of the elementary composition of the ions the following direction of the decomposition of M^+ of heliotrine (X) is shown:

$$X,\ 313\,(M^+) \xrightarrow[-CO;\ -C_3H_7CO]{*} 214\,(3) \xrightarrow[-CH_3OCH=CH_2]{*} 156\,(12).$$

It has been reported that neither type of decomposition is observed in the spectra of alkaloids with an unmethylated secondary OH group, such as echinatine (XI), although this has the peak of an ion with m/e 156. On the other hand, it has been established [8] that the spectrum of methyltrachelanthamine (XII) shows the peaks of ions with m/e 183, 200, and 142, corresponding to the peaks of ions with m/e 197, 214, and 156 in heliotrine (X). Consequently, the $C_1=C_2$ π bond is not the cause of the migration of the CH_3CHOCH_3 radical to the pyrrolizidine nucleus.



Scheme 5



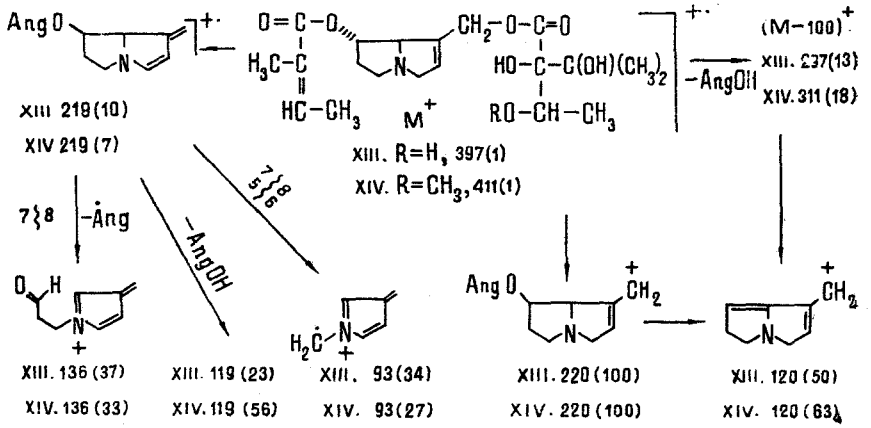
Scheme 6

The idea of the migration of elements of the side chain to the nitrogen atom of the nucleus (Scheme VI) combines cases of the migration of the radicals R and CH_3CHOCH_3 and satisfactorily explains the subsequent stage of the elimination of the $CH_3OCH=CH_2$ molecule for the ions with m/e 214 (X) and 200 (XII), and also of a ketene molecule from an ion with m/e 184 ($C_{10}H_{18}O_2N$) in the spectrum of trachelanthamine acetate (VIII), which leads to an ion with m/e 142 ($C_8H_{16}ON$) [5].

Diester Alkaloids. To evaluate the influence of the second substituent attached by an ester bridge to C_7, Pedersen and Larsen [2] studied the spectrum of 7-angeloylheliotridine and 7-angeloylretronecine. The first two methods of fragmentation of these compounds consisted in the splitting out of the angelic acid molecule [$(M - 100)^+$ ions] or the angeloyl radical [$(M - 83)^+$ ions].

In the spectra of the diester alkaloids heliosupine (XIII) and lasiocarpine (XIV), the allyl cation with m/e 220 is the 100% ion [2]. The peak of the $(M - 100)^+$ ion has an intensity considerably lower than that of this ion, which serves as the main difference in the spectra of these alkaloids from the diester bases with a platynecine skeleton. The methods

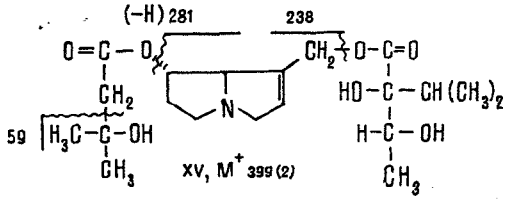
of splitting off of the substituent from C_7 given above are reflected in the processes of formation of ions with m/e 120, 119, and 136 (Scheme 7).



Scheme 7

In contrast to heliosupine (XIII) and in analogy with heliotropine (X), the spectrum of lasiocarpine (XIV) has low-intensity fragments with m/e 279 (197 + 82), 238 (156 + 82), and 296 (214 + 82), showing the migration of the CH_3CHOCH_3 to the pyrrolizidine nucleus.

The laws of the fragmentation of the diester alcohols with the heliotridine skeleton have served as a basis for determining the structure of symphytine [24] and of uluganine (XV) [25]. The spectrum of uluganine (XV) (M^+ = 399) contains the peaks of ions with m/e 136, 120, 93, and 80, which are characteristic of bases with the heliotridine skeleton. In place of the peak of an ion with m/e 220 from lasiocarpine (XIV) there is the 100% peak of an ion with m/e 238. The weak peak of an ion with m/e 220 is connected with that having m/e 238 by the loss of a molecule of water. Consequently, the OH at C_7 may be esterified by a C_5 acid with a hydrated double bond, as is confirmed by the presence in the spectrum of (XV) of the ion $(M - 118)^+$ with m/e 281. The mass number of the residue esterifying C_9 is 399 − 238 = 161 a.m.u., which corresponds to viridofloric or trachelanthic acid. This is confirmed by the presence of a triplet of ions with m/e 354-356 (analogous to the cation with m/e 240-242 of the bases (VII)). On the other hand, the spectrum of uluganine has a peak with m/e 59 (30%) which is absent from the spectrum of (VII) and from that of heliosupine (XIII). On the basis of this fact, it has been suggested that the substituent at C_7 includes a hydroxyisopropyl group. In combination with the results of other methods, it has been established that uluganine (XV) possesses a heliotridine skeleton esterified with trachelanthic and β-hydroxyisovaleric acids:

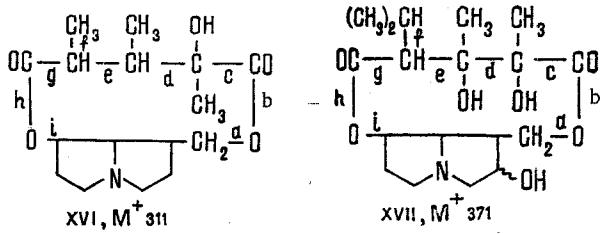


Fragmentation of Alkaloids with an 11-Membered Macrocycle

Platynecine Group. A common property of the macrocyclic pyrrolizidine bases is the increased stability of the molecular ions in comparison with alkaloids having an open side chain. At the same time, the spectrum of retusine (XVI) [10], which is based on the platynecine stereoisomer turneforcidine [9], an analogy is shown with sarracine (IX) which consists in a tendency to decomposition of the pyrrolizidine nucleus and the formation fragments with m/e 82 (100%), 95, and others. In the spectrum of croalbidine (XVII) with an OH group at C_2 [11], in addition to m/e 82 there is the strong peak of an ion with m/e 98 (82 + 16). This reflects the participation of rings A and B in fragmentation.

It is impossible to establish a definite rule in the decomposition of the macrocyclic rings (XVI) and (XVII) from the facts given by the authors concerned [9, 10]. We may note

only the appearance in the specta of ions with m/e 211 (XVI) and 227 (XVII) arising as the result of *id* cleavage.



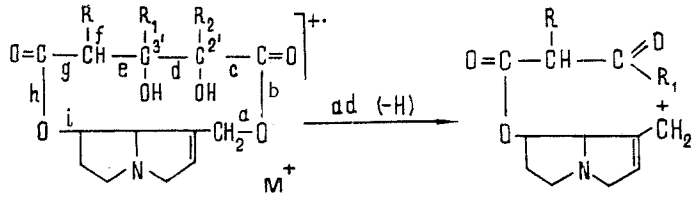
XVI, M^+ 311 XVII, M^+ 371

Retronecine Group. The spectra of esters of retronecine (Va) and substituted glutaric acids are characterized by the same set of peaks as the diester alkaloids (XII-XV) — m/e 136, 120, 119, and 93. Because of this, the analysis of the fragmentation of the macrocycle acquires greater importance. With monocrotaline (XVIII) as an example, a characteristic feature has been established [1] — *ad* cleavage with the migration of one hydrogen atom to the neutral fragment (ion with m/e 236).

On comparing the mass numbers of the M^+ ions and the analogs of the fragments with m/e 236 in the spectra of junceine (XX), axillarine (XXI), and axillaridine (XXII) with the corresponding characteristics of trichodesmine (XIX), Atal [26] and Crout [27] determine the nature of the substituent at $C_{3'}$ of the alkaloids (XX-XXII) (Scheme 8).

It must be mentioned that in the spectra of the bases with the platynecine skeleton (XVI, XVII), ions of this type have a low intensity or are absent.

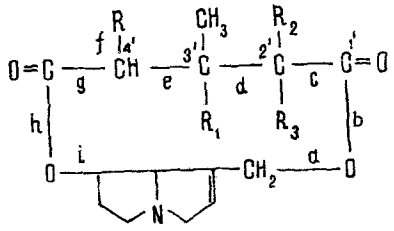
Two cases are known of deviations from the law of the fragmentation of the macrocycles of alkaloids with retronecine skeleton. The region of high mass numbers of the spectrum of incanine (XXIII) [28] is rich in peaks of medium intensity, and here the *ad* cleavage is not the predominating process of fragmentation [29]. Some of the characteristics are possessed by the spectrum [27] of crispatine (XXIV) [30], while its stereoisomer at $C_{3'}$ — fulvine (XXV) [31] — in its behavior under electron impact [27] is classed with monocrotaline (XVIII) and trichodesmine (XIX) [29]. Scheme 9 shows fragmentation analogies found for representatives of the two groups of compounds [for 100% were taken the maximum peaks in the $M^+ - 160$ m/e region; (+H) denotes the migration of a hydrogen atom to the charged fragment and (−H) to the neutral fragment].



	R	R_1	R_2		
XVIII.	CH_3	CH_3	CH_3	325(10)	XVIII. 236(72)
XIX.	i-C_3H_7	CH_3	CH_3	353(8)	XIX. 264(100)
XX.	i-C_3H_7	CH_3	CH_2OH	369	XX. 264
XXI.	i-C_3H_7	H	$CH(OH)CH_3$	369	XXI. 250
XXII.	i-C_3H_7	H	C_2H_5	353	XXII. 250

Scheme 8

It can clearly be seen that processes that include the cleavage of the *d* bond predominate in the first group. The decomposition of compounds of the second group begins mainly with the elimination of CO_2 (*ac* cleavage) and the contraction of the macrocycle. Since the OH group in the molecules compared is present on different carbon atoms of the macrocycle, two types of analogies are observed in the spectra of incanine and crispatine: with respect to the position of cleavage of the chain and with respect to the composition of the fragments ejected. The latter are shown in the lower part of the right-hand column of Scheme 9.



	R	R_1	R_2	R_3	M^+
XVIII	CH_3	OH	CH_3	OH	325 (14)
XIX	$i-C_3H_7$	OH	CH_3	OH	353 (8)
XXV	CH_3	OH	CH_3	H	309 (19)

Type of cleavage	m/e (%)	
	XIX	264 (100)
ad (−H)	XVIII	236 (100)
	XXV	236 (100)
	XIX	220 (6)
		222 (3)
ae	XVIII	193 (6)
	XXV	193 (22)
bd	XIX	281 (8)
	XXV	253 (16)
id	XIX	209 (9)
	XXV	193 (22)

	R	R_1	R_2	R_3	M^+
XXIII	$i-C_3H_7$	H	OH	CH_3	337 (89)
XXIV	CH_3	OH	H	CH_3	309 (25)

Type of cleavage	m/e (%)	
ac	XXIII	293 (24)
	XXIV	265 (25)
ad (+H)	XXIII	250 (59)
	XXIV	238 (15)
ad (−H)	XXIII	248 (16)
	XXIV	236 (26)
ae (+H)	XXIII	222 (100)
	XXIV	194 (43)
bd (−H)	XXIII	264 (26)
ad (−H)	XXIV	236 (26)
ac+*ad* (+H)	XXIII	250 (59)
ac+*de* (+H)	XXIV	222 (100)

Scheme 9

The main directions of decomposition of trichodesmine and incanine were confirmed by a measurement of the elementary composition of the ions [8, 23]. The ion with m/e 250 (XXIII) proved to be composite. It is formed not only by the *ad* cleavage but also as the result of the splitting out of CO_2 and C_3H_7 from M^+, which reflects the contribution of the isopropyl group at $C_{4'}$. On the basis of the analogies found, Atal et al assumed that the methyl groups $C_{2'}$ and $C_{3'}$ in incanine and crispatine were present in the transoid, and in fulvine in the cisoid, configuration. In subsequent x-ray structural investigation of fulvine [53] and axillarine [54] it was shown that it is almost pointless to speak of a cisoid or transoid orientation of these groups. Nevertheless, the statement of the presence of two stereoisomeric series of macrocyclic alkaloids with different mass-spectrometric properties [8, 29] remains in force.

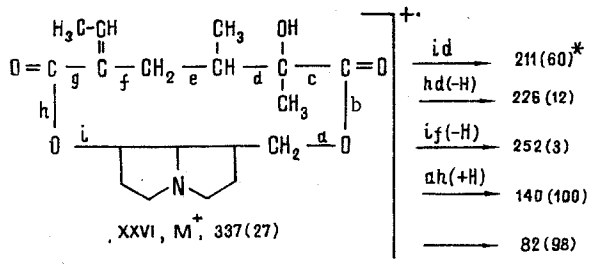
Fragmentation of Alkaloids with 12-Membered Macrocycles

Platynecine Group. Culvenor et al. [9] have given the relative intensities of the main fragments in the spectra of platyphylline (XXVI) and its isomer with respect to the necine nucleus — hastacine — and that with respect to the esterifying acid — neoplatyphylline. Here, the process of forming the ion with m/e 82 plays the same important role as in the cases of the other platynecine bases. Ions characteristic of them with m/e 138, 123, 122, and 95 also appear in the form of strong peaks. An increase in the contribution of the fragments with m/e 140 and 96 distinguishes the spectra of the platynecine isomers from the spectra of the diester bases with an open chain. It is possible that the first of them is the 7-hydroxy analog of the m/e 124 ion of viridiflorine and its isomers (VII), and the second is formed from the first by C_7-C_8 and C_5-C_6 cleavage and the elimination of a molecule of acetaldehyde. The deuteration of platyphylline [2] confirmed this version.

An analysis of the fragmentation of the macrocycle of platyphylline (XXVI) in comparison with the decomposition of the retronecine bases has been given previously [32]. It has been established that for (XXVI) the cleavage of the bonds of the ester group at C_7 becomes still more characteristic than for the alkaloids with an 11-membered macrocycle of the type of retusine (XVI). The peak of the ion with m/e 211 corresponding to the *id* cleavage is far stronger than all the peaks in the region of high mass numbers of the spectrum of (XXVI). Together with this peak there are the peaks of ions with m/e 226 and 252 characterizing the *hd* and *if* cleavages (Scheme 10; the relative intensities given have been taken from the paper of Culvenor et al. [9]).

So far as concerns decomposition processes with the participation of the ester group at C_9, the spectrum of (XXVI) shows peaks of fragments with m/e 222 [*ad*(+H)], 266 [*bd*(+H)], and 293 $(M - CO_2)^+$. The decomposition scheme suggested for (XXVI) is confirmed by the spectrum of its OD analog.

The presence of ions with m/e 82, 122, 123, and 138 in combination with information on their elementary composition has permitted the determination of the platynecine nature of the alkaloid nemorensine [33] which has an unusual 13-membered macrocycle.



Scheme 10

Retronecine Group. The mass spectra of the alkaloids with 12-membered macrocycles at the retronecine nucleus have been considered by Atal et al. [34] using as examples senecionine (XXVII) and anacrotine (XXVIII) [34]. Together with the appearance of the peaks of ions with m/e 136, 120, 119, and 93 that are typical for the retronecine bases (XXVII) and the 6-hydroxy analogs of the first three peaks (XXVIII), the intensities of the more saturated fragments with m/e 138, 121, 95, and 94 have increased.

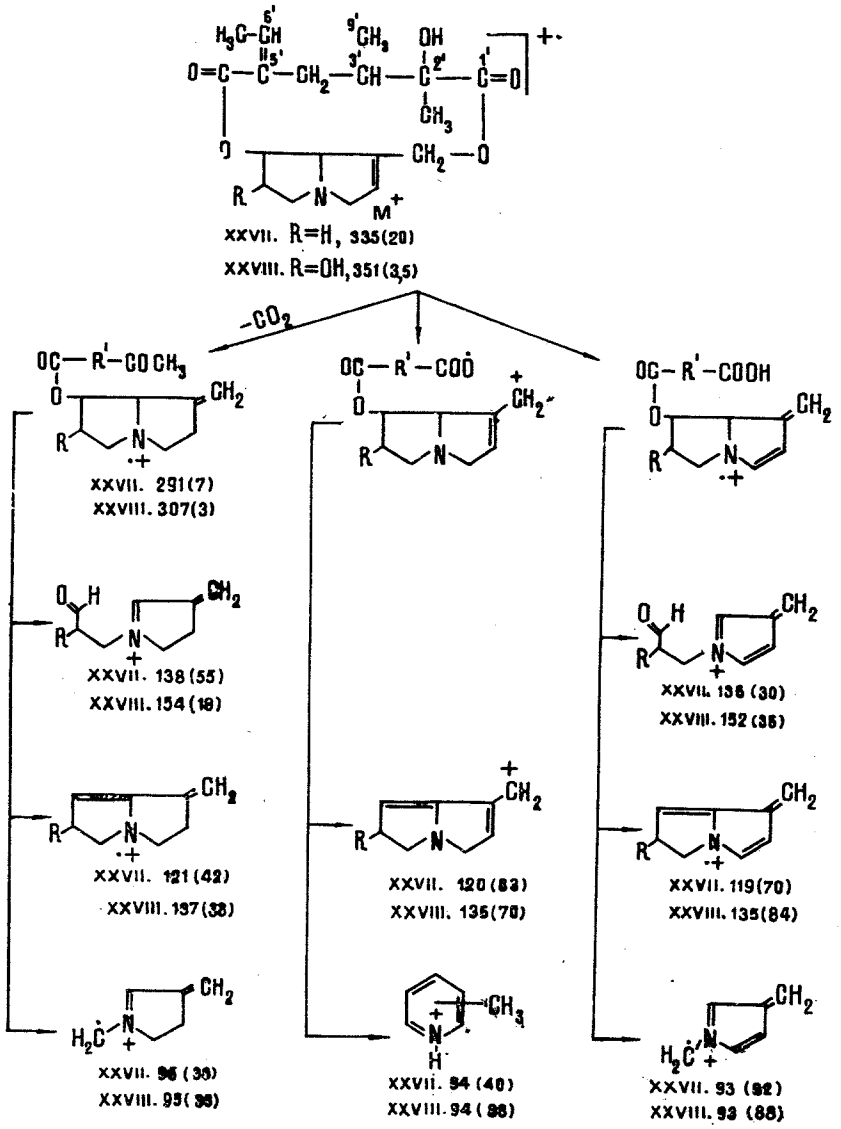
Atal et al. [34] have suggested that in all cases the $C_9 - O$ bond is cleaved first, and the doublets or triplets of peaks are formed as the result of the migration of the hydrogen macrocycle into the necine nucleus or conversely, or without rearrangements (See Scheme 11 on the following page).

In a number of cases, the presence of peaks with m/e 136, 120, 119, 93 has served as a basis for the identification of the retronecine nucleus of alkaloids with 12-membered macrocycles [27, 35, 36]. However, use of the results of mass spectrometry for the purpose of determining the structure of the macrocycle was limited to showing the presence of the ions $(M - 44)^+$ and $(M - 45)^+$ [35, 37] formed by *ac* cleavage, and of an ion with m/e 220 [37, 38], apparently arising as the result of *ae* cleavage. Nevertheless, these fragments are insufficiently specific for alkaloids with 12-membered macrocycles. The *ac* cleavage is characteristic for a number of bases with 11-membered rings — and the ion with m/e 220 appears in the spectrum of the triester alkaloids with the heliotridine nucleus (XII-XV). Consequently, to judge the size and structure of the macrocycle its fragmentation must be analyzed simultaneously in all directions taking each of them into account.

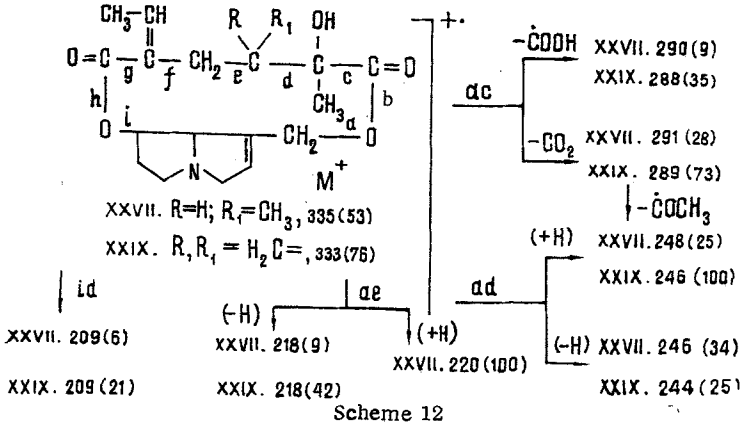
Thus, a comparison of the spectra of senecionine (XXVII) and seneciphylline (XIX) (Scheme 12), which differs from (XXVII) by the presence of the $C_3'=C_9'$ double bond, has shown [32] that the latter activates *c* cleavage, because of which in the spectrum of (XXIX) the peaks of the ions $(M - CO_2)^+$ and $(M - COOH)^+$ are stronger. The formation of the main ion with m/e 246 in this region of the spectrum of (XXIX) also takes place through a stage of the ion with $(M - CO_2)^+$. In the absence of a $C_3'=C_9'$ bond, the cleavage *e* is more favorable and therefore the ion with m/e 220 of the senecionine spectrum is the maximum ion in the region of high masses.

The difference in the degrees of saturation of the $C_3' - C_9'$ bond also explains the difference in the tendency to the *id* cleavage. If the main directions of the fragmentation of the macrocycles are known, a simple analysis of the mass numbers of the fragments gives a considerable amount of information. (See Scheme 12 and Scheme 13 on the following pages.)

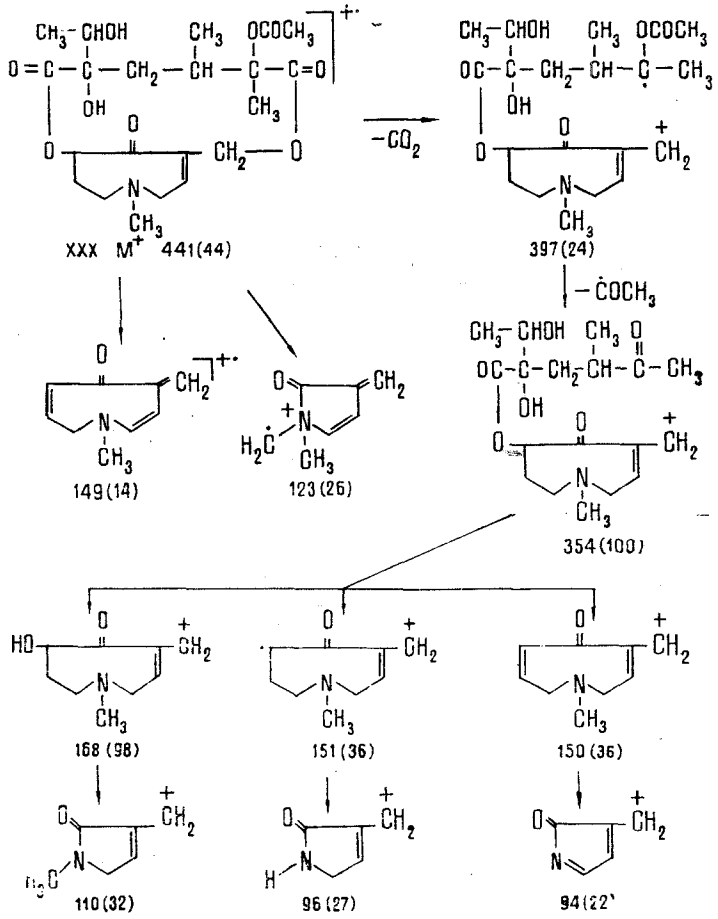
Otonecine Group. The mass spectra of the otonecine bases are characterized by an increase in the contribution of the ions formed by the elimination of the fragments of the macrocycle, which is possibly explained by a decrease in the probability of the localization of the charge on the nitrogen atom. The basic properties of the spectra of these compounds have been given by Atal [39] in connection with the connection of floridanine (XXX), florosenine, and floricaline in plants of the genus *Cacalia*. The main fragment of the pyrrolizidine nucleus with m/e 168 (Scheme 13) has the structure of an allyl cation and is strictly



Scheme 11



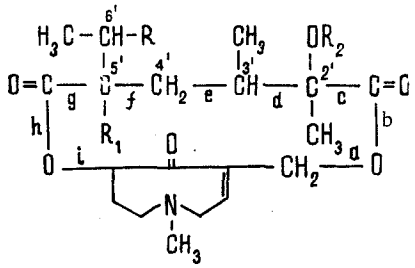
Scheme 12



Scheme 13

specific for bases of this type. Fragments with m/e 151-149, 123, and 110 are essentially analogous to the ions characteristic for the retronecine bases (XXVII) and (XXIX) (m/e 121-119, 93, 80). In the case of floridanine (XXX), Cava et al. [39] report a high intensity of the peak of the ion $(M - 44)^+$, further decomposing by the elimination of an acetyl radical from C_2'–O (see Scheme 13). A similar type of decomposition has been observed in the spectrum of clivorine [40] having at C_2' the same substituents (XXX), and together with them are observed the peaks of the ions $(M - CH_3COO)^+$ and $(M - CO_2 - CH_3COO)^+$. By comparing the spectra of renardine (XXXI) and hydroxyrenardine with the spectrum of cratofoline Crout [41] determined the structure of the latter as 2'-demethylrenardine. In all three spectra he found ions with m/e 250 analogous to the ions with m/e 220 of senecionine (XXVII) (*ae* cleavage).

By analyzing the fragmentation of the macrocycles of the otonecine bases the authors [42] divided these compounds into two subgroups according to number of oxygen functions in the macrocycle. In the first subgroup, including renardine (XXXI) and otonecine (XXXII), there is an increased tendency to ring-closure at bond *b* (*bc*, *bd*, and *be* cleavages) and the role of processes of the participation of bond *a* has decreased, with the exception of the formation of the ion $(M - CO_2)^+$. The presence of an epoxide bridge at C_5'–C_6'(XXXII) corresponds to the *af* cleavage which is absent in the case of renardine. The peaks of ions of medium intensity with the coincident mass numbers 238 (*id*), 254 (*hd*), and 266 (*ie*) are formed by the cleavage of the bonds of the ester group at C_7.



XXX. R=R_1+OH, R_2=$COCH_3$

XXXI. R–R_1=$\Delta^{5',6'}$, R_2=H

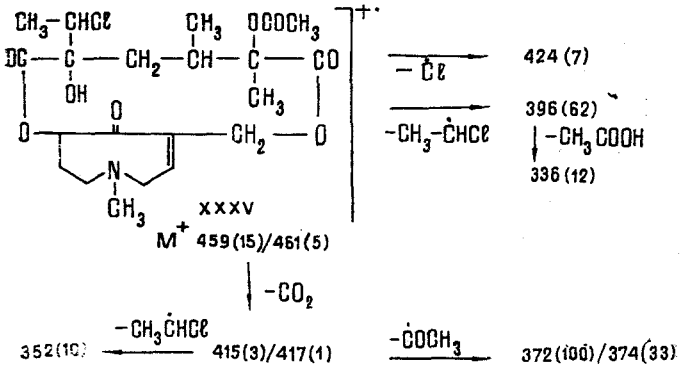
XXXII. R+R_1=O, R_2=H

XXXIII. R=$OCOCH_3$, R_1=OH, R_2=$COCH_3$

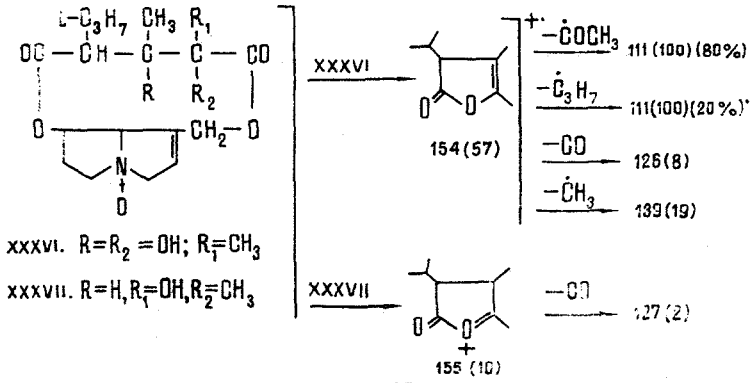
XXXIV. R=$OCOC_2H_5$, R_1=OH, R_2=$COCH_3$

The second subgroup includes derivatives of floridanine (XXX) — floricaline (XXXIII) and floridanine propionate (XXXIV). These compounds are distinguished by their capacity for fragmentation of the substituents at C_2' and C_5' and by the decrease in the contribution of the cleavages of bonds *d*, *e*, and *f*. On measuring the elementary composition of fragment (XXX) it was found that the ions $(M - 44)^+$ consist of $(M - CO_2)^+$ to the extent of only 35%, and 65% of the ions correspond to the elimination of a CH_3CHO molecule from M^+ through the substituent at C_5'. The ion with m/e 338 is also a doublet, the components of which correspond to $[M - CO_2 - OCOCH_3]^+$ (40%) and $[M - CH_3CHO - OCOCH_3]^+$ (60%). So far as concerns the fragments arising by the decomposition of the ester group at C_7, cleavages *ie* and *hd* lead to peaks of low intensity, and cleavage *id* is accompanied by the elimination of the acetyl radical from C_2'-O with stabilization of the ions produced with m/e 238 in the cyclic form. Apparently, these ions are analogous to those of the same mass in the spectra of renardine and otosenine.

The characteristic feature of the fragmentation of the macrocycle of the otonecine bases that has been found has proved useful in determining the structure of the chlorine-containing alkaloid doronine (XXXV) [43] — a chlorohydrin derivative of florosenine (Scheme 14).



Scheme 14



Scheme 15

The N-Oxides of the Pyrrolizidine Alkaloids accompany the free bases in plants and sometimes are present in greater amounts [20]. The mass spectra of these compounds were not specially studied before the work of U. A. Abdullaev [8]. Bild and Hesse [44] have studied the spectra of the N-oxides of a series of saturated heterocyclic compounds and have established the presence of a triplet of peaks of the ions at $(M - 16)^+$, $(M - 17)^+$, and $(M - 18)^+$. The first of the ions corresponds to the molecular ion of the free base and is formed by the thermal decomposition of the N-oxide molecule [45]. By the bulk deuteration of some N-oxides it has been established that the OH group of the side chain does not participate in the formation of the $(M - 17)^+$ and $(M - 18)^+$ ions and the OH and H_2O fragments are formed from the oxygen of the N→O group and the hydrogens of the pyrrolizidine nucleus [8, 46]. In these investigations, the spectra of a total of 12 N-oxides of amino alcohols and alkaloids with the heliotridane, heliotridine, platynecine, and retronecine skeletons were studied. The peaks of molecular ions were found to have a low intensity in the spectra of the N-oxides of the amino alcohols and alkaloids of the trachelanthamidine series. The fragments observed in the spectra of the N-oxides have been subdivided into three types: A — ions characteris-

tic of the natural bases; B — ions formed from the ions $(M - 17)^+$ and $(M - 18)^+$; and C — ions retaining the oxygen atom of the N→O group in their composition.

The mass numbers of ions of type B are 2-4 m.u. smaller than the ions of type A. Fragments coinciding in their mass numbers with the fragments of type B are also observed in the spectra of the partially dehydrogenated pyrrolizidines [47], which confirms the conclusion concerning the nature of the $(M - 17)^+$ and $(M - 18)^+$ ions. It has also been shown [46] that the $(M - 18)^+$ atoms are not the consequence of thermal dehydration. In the spectra of the N-oxides of bases with a retronecine skeleton the height of the peaks of ions of type B exceed the heights of the peaks of ions of type A.

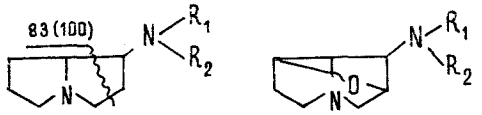
Ions of type B, shifted by 16 amu in the direction of higher masses as compared with the ions A have been detected only in the spectra of the N-oxides of trachelanthamidine and its esters. It is assumed that the ions of this type arise as the result of rearrangement processes taking place under mass-spectrometric conditions, the first stage of which is the formation of a covalent bond between the oxygen of the N→O group and the α-carbon atom of the heterocycle. This hypothesis is based on a number of facts, one of which is the observation in the spectrum of quinoline N-oxide of fragments characteristic for 2-quinolone [48]. (See Scheme 15 on previous page.)

In the N-oxides, the probability of the localization of the charge on the nitrogen atom has decreased, in view of which the contribution of the nitrogen-free fragments increases. This is shown to the greatest extent in the spectrum of trichodesmine N-oxide (XXXVI) [46]. The appearance of an ion with m/e 154 having the composition $C_9H_{14}O_2$ and its subsequent decomposition (Scheme 15) shows that it has the structure of a dehydrated deacyl cation of a lactone acid. For incanine N-oxide (XXXVII), an ion with m/e 155 ($C_9H_{15}O_2$) coinciding in its structure with the ion of the same mass in the spectrum of the incanine lactone acid [21] is more characteristic.

In a paper on the proof of the structure of anadoline (3'-tigloylechinatine N-oxide) [51, 52], unpublished results of Edgar and Culvenor are mentioned that show a similarity of the spectra of the tertiary bases and their N-oxides and the appearance in the spectra of the latter of the ions $(M - 16)^+$ and $(M - 18)^+$.

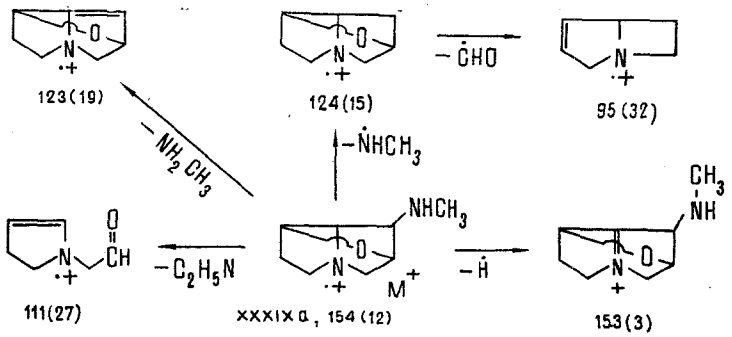
Fragmentation of 1-Amino Pyrrolizidine Derivatives

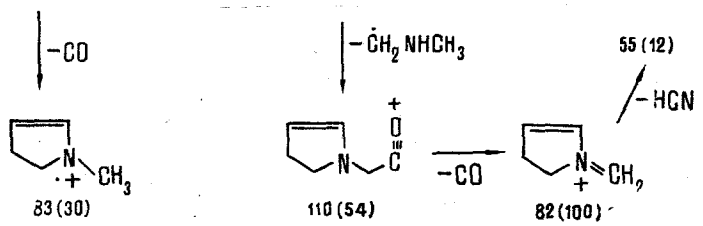
The molecular ions of alkaloids of this type have even mass numbers [49]. By the nature of their fragmentation these bases and their derivatives can be divided into two subtypes: (XXXVII) and (XXXIX). The first subtype includes, apart from the alkaloid laburnamine [1], synthetic derivatives of loline [49] the fragmentation of which takes place similarly to that of the amino alcohol trachelanthamidine (Ib), giving the maximum peak in the spectrum with m/e 83.



XXXVIII XXXIX

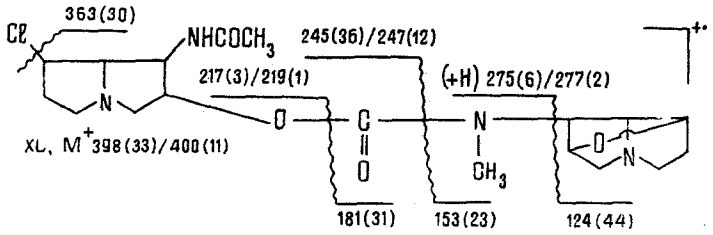
Because of the presence of the C_2-O-C_7 bridge, the fragmentation of compounds of the subtype (XXXIX) takes place by a peculiar mechanism [49]. Ions with m/e 82 (100%) coincide in their structure with the corresponding ions of platynecine (III). In addition, the spectra are characterized by stable atoms with m/e 124, 123, 111, 110, and 95, with the methods of forming which are shown in Scheme 16 for the case of loline (XXXIXa).





Scheme 16

Mass spectrometry in combination with IR and NMR spectroscopy has been used successfully to determine the structure of the dimeric chlorine-containing base loiidine (XL) [50].



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