UDC 547.944/945

MASS-SPECTROMETRIC STUDY OF THE STRUCTURE OF THE ALKALOIDS OF LOLIUM

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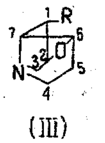
Khimiya Prirodnykh Soedinenii, Vol. 4, No. 5, pp. 298–304, 1968

Studying the chemical and physical properties of the alkaloids norloline (III), loline (IV), and lolinine (V), we have proposed the following structures for them and the products of their transformation [1,2]:

(I) $R=H$
(II) $R=OH$
(III) $R=NH_2$
(IV) $R=NHCH_3$



(III)

(V) $R=N{<}^{CH_3}_{COCH_3}$
(VI) $R=N{<}^{CH_3}_{CH_3}$
(VII) $R=N{<}^{CH_3}_{COC_6H_5}$

From formula (III), the formula follows for dihydrodeoxyloline (VIII) and for N-methyldihydrodeoxololine (IX)

(VIII) $R_1=N{<}^{H}_{CH_3}$

(VIII)

(IX) $R_1=N{<}^{CH_3}_{CH_3}$

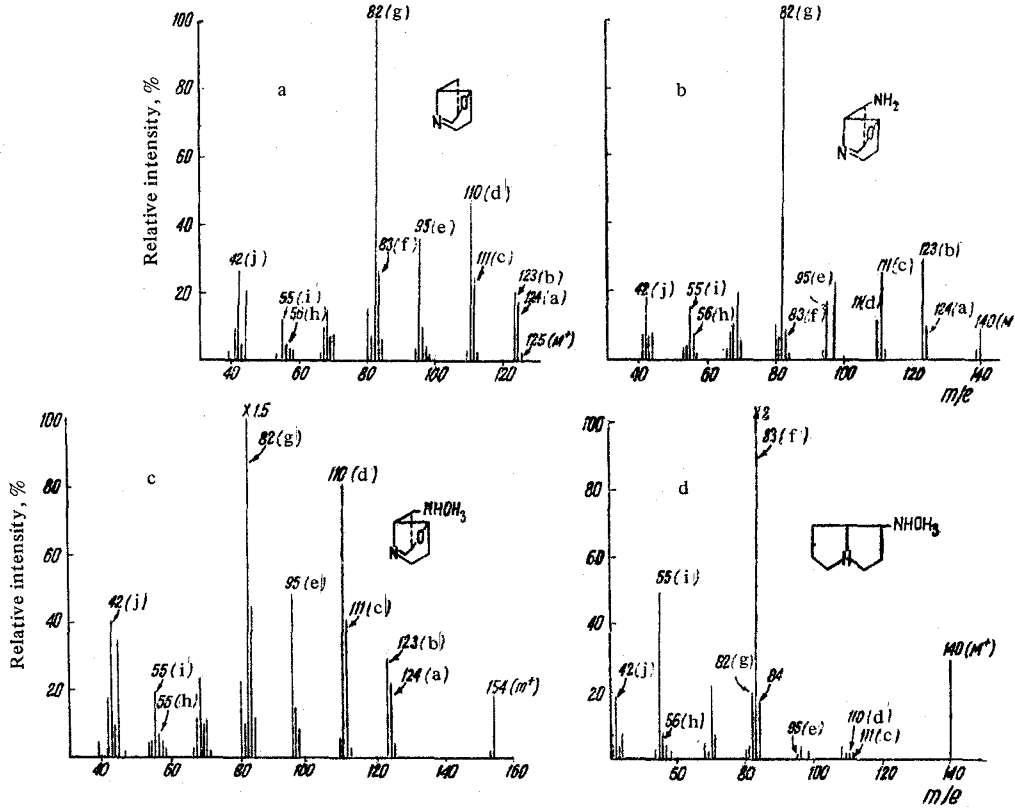
Mass-spectrometric studies of alkaloids of the pyrrolizidine series [3, 4] and their amino alcohols [5], and the mass spectrum of an isomer of loline—festucine [6]—have been reported previously. However, there is no information on the fragmentation of festucine. What has been said above as well as a complex of alkaloids of lolium and the products of their transformation have enabled us to study the properties of the substances by mass spectrometry.

Substance	m/e (relative intensity, %)					
	M^+	*a*	b	c	d	e
(I)	125 (2)	124 (18)	123 (20)	111 (25)	110 (48)	95 (36)
(II)	141 (32)	124 (23)	123 (3)	111 (2)	110 (2,5)	95 (56)
(III)	140 (11)	124 (10)	123 (31)	111 (26)	110 (14)	95 (17)
(IV)	154 (18)	124 (22)	123 (29)	111 (41)	110 (81)	95 (48)
(V)	196 (7)	124 (13)	123 (35)	111 (4)	110 (4)	95 (45)
(VI)	168 (11)	124 (52)	123 (93)	111 (12)	110 (6)	95 (96)
(VII)	258 (6)	124 (11)	123 (32)	—	—	95 (35)
(VIII)	146 (30)	—	—	111 (2)	110 (2)	95 (1)
(IX)	154 (83)	—	—	111 (4)	110 (6)	95 (6)

Substance	m/e (relative intensity, %)				
	f	g	h	i	j
(I)	83 (27)	82 (100)	56 (5)	55 (12)	42 (9)
(II)	83 (20)	82 (100)	56 (7)	55 (25)	42 (17)
(III)	83 (9)	82 (100)	56 (8)	55 (16)	42 (18)
(IV)	83 (45)	82 (100)	56 (7)	55 (19)	42 (41)
(V)	83 (15)	82 (100)	56 (16)	55 (8)	42 (20)
(VI)	83 (14)	82 (100)	56 (9)	55 (2)	42 (90)
(VII)	83 (9)	82 (70)	56 (13)	55 (15)	42 (11)
(VIII)	83 (100)	82 (20)	56 (8)	55 (50)	42 (19)
(IX)	83 (100)	82 (52)	56 (9)	55 (87)	42 (33)

The present paper gives the main results of a study of the mass spectra of nine substances. The fragmentation of these substances under electron bombardment showed that the ionization of the molecule takes place most probably through the expulsion of one electron from the unshared pair of electrons of the nitrogen atom at the nodal point of two condensed rings. In spite of the fact that some of the m/e values given in the table are the same, they correspond to ions of different structures.

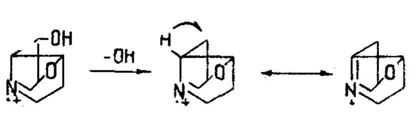
It can be seen from the table that in the mass spectra of compounds (I)–(VII) and (VII')–(IX) fragmentation takes place exclusively in one direction. This direction of decomposition is natural, since the substances investigated are based on the same heterocyclic nucleus. The difference in the mass spectra of compounds (I)-(IX) consists in the appearance of some specific fragments formed by a change in the functional groups in the C_1 position of the pyrrolizidine ring where the side-chain nitrogen atom and the other groups are located. Hemiloline (I) was obtained by the usual method by diazotizing substance (III) in hydrochloric acid solution in the presence of univalent copper with subsequent Raney nickel reduction.



Mass Spectra of Hemiloline (a), Norloline (b), Loline (c), and Dehydrodeoxyloline (d).

In substance (I) the ionization of the molecule takes place with the formation of a molecular ion peak of low intensity (2% of the maximum) (figure, a). The first act of fragmentation of the molecular ion begins with the formation of the ions *a* (M-1) and b(M-2), arising as the result of the detachment of one of the two hydrogen atoms, these being 9-10 times more intense than the peak of the molecular ion. The further fragmentation of the molecular ion of (I) (see table) takes place with the formation of the fragments c, d, e, f, g, h, i, and j.

In the spectrum of heminorloline (II), the fragment M-17 is more characteristic than M-18, the ion-radical *a* obviously passing into a more stable form—the ion *a'*—with the migration of a hydrogen atom from C_7 of the molecule (II) to C_1.



(II) M^+ 141 *a*, m/e 124 *a'*

In contrast to the mass spectra of substances (I) and (III)-(VI), in heminorloline (II) the fragment c is of low intensity and amounts to only 2% of the maximum peak. The fragment e is obtained from the ion-radical *a* with the loss of a CHO group. It is possible that this type of α, β-rupture is energetically more favorable for the ion *a* than for the stable ion *a'*.

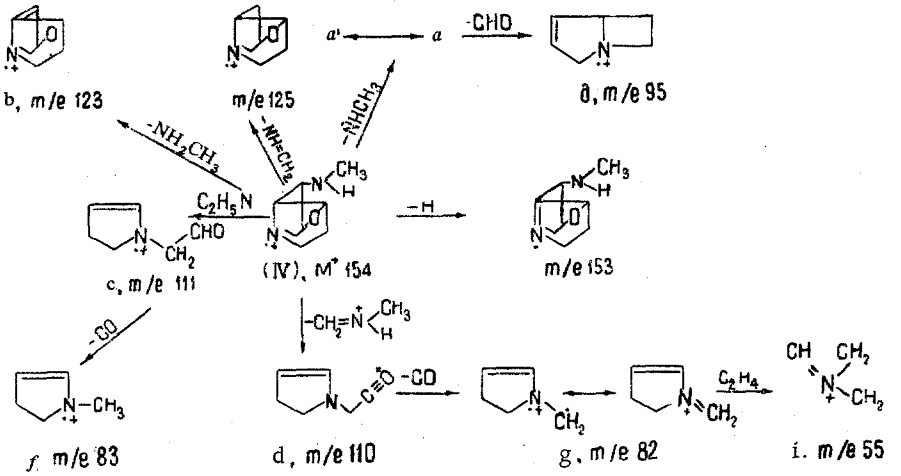
In the mass spectrum of norloline (III) (figure, b) there is a fragment M-1 arising as the result of the detachment of the hydrogen atom, possibly from C_7, while the fragment M-29 may be formed by the expulsion of a CHO or a $CHNH_2$ group. Since the peak of the ion with m/e 111 is found in the spectra of compounds (I), (II), and (IV)-(VII), the detachment of a CHO group from the molecular ion (III) is unlikely.

In the formation of fragment c, the α,β-ruptures of the C_1—C_7, C_1—C_2 bonds, the C_6—O ether bridge take place successively.

A series of transitions (b, d, e, *f*, i; see table) in the mass spectrum of (IV) is confirmed by metastable peaks, for example the transitions:

$M^+ \to b$, $M^+ \to d$, $a \to e$, $c \to f$, $g \to i$.
$m^+ = 98.2$, for $154 \to 123$ calculated 98.2,
$m^+ = 78.6$, for $154 \to 110$ calculated 78.6,
$m^+ = 72.7$, for $124 \to 95$ calculated 72.7,
$m^+ = 60.4$, for $111 \to 83$ calculated 60.4,
$m^+ = 37$, for $82 \to 55$ calculated 37.

In the spectrum of (IV), as in (I) and (III), there is a M-1 peak of low intensity. The formation of the ion b is more favorable than fragment *a* and particularly than the fragment with m/e 125 (figure, c). Fragment *a* is formed directly from the molecular ion by the elimination of the side-chain nitrogen atom. One of the high-intensity peaks of the ions is the fragment d with m/e 110. The fragment with m/e 95 arises from the ion with m/e 124 by the expulsion of a —CHO group. The ion with m/e 83 in compounds (I)–(VII) is less intense than the ion formed from (VIII) and (IX) and arises from the ion with m/e 111. This course of the fragmentation is natural since in compounds (VIII) and (IX) there are no functional groups in the C_6—C_2 position. The ion with m/e 82 is the most intense fragment in the mass spectrum of (I)–(VI). Although the formation of fragment g with m/e 82 was not shown by the existence of metastable peaks, it arises from the ion with m/e 110 as the result of the expulsion of the element CO.

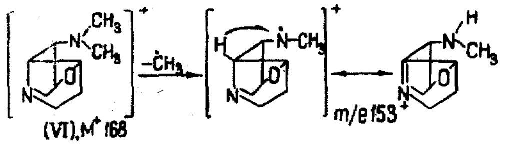


In the case of N-methylloline (V), in addition to the maximum ion with m/e 82 there are intense peaks of ions with m/e 123 and m/e 95 which have low intensities in the mass spectra of (I)–(IV), (VI), and (VII). Apparently, the N-methyl group has a strong influence on the fragmentation of the molecule of (V), particularly in the formation of the ions with m/e 123 and 95. The same feature is observed in the mass spectrum of N-methyldihydrode oxyloline.

The transitions $M^+ \to b$ and $b \to e$ are confirmed by the metastable peaks

$m^+ = 90.3$, for $168 \to 123$ calculated 90.3,
$m^+ = 73.5$, for $123 \to 95$ calculated 73.5.

Some of the distinctive fragments in the mass spectra of (V), (VI), and (VII) are the peaks with M-43, M-15, and M-105, which are formed by the detachment from the molecular ion of acetyl, methyl, and benzoyl groups, respectively, and the migration of an atom of hydrogen from C_7 to the side-chain nitrogen atom.

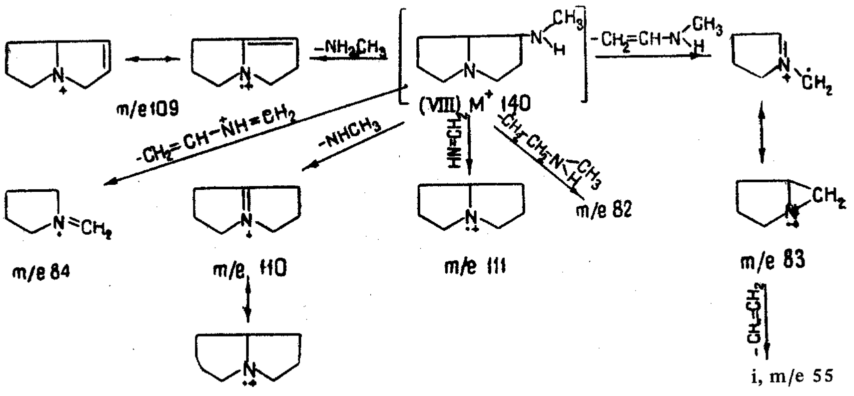


In the mass spectrum of N-benzoylloline (VII), the maximum peak is that of the fragment with m/e 105 and not the peak with m/e 82 as might have been expected. The ion with m/e 105 corresponds to the benzoyl ion, which is shown by the further degradation of the ion with the formation of an intense peak of the phenyl cation with m/e 77.

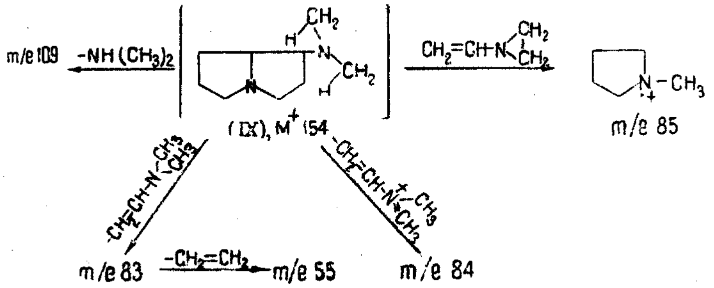
The spectra of dihydrodeoxyloline (VIII) (figure, d) and of N-methyldihydrode oxyloline (IX) proved to be the simplest. In the mass spectrum of (VIII) and (IX) the peak of the ion with m/e 83 has the maximum intensity. The formation of fragment f was to be expected, since the oxygen bridge of the alkaloid (IV) in the C_6–C_2 position is replaced by hydrogen atoms. Naturally, the first act of fragmentation will be the α,α-rupture of the molecular ion of (VIII) with the formation of fragment f. The transitions from the molecular ion in (VIII) to the fragment f, and also $f \rightarrow$ i, are confirmed by the metastable peaks

$$m^+ = 49.2, \text{ for } 140 \rightarrow 83 \text{ calculated } 49.2,$$
$$m^+ = 36.6, \text{ for } 83 \rightarrow 55, \text{ calculated } 36.6.$$

In compounds (VIII)–(IX), the fragment with m/e 83 in the ionic form possibly appears differently from the ion with the same value of m/e appearing in the mass spectra of (I)–(VII), since in the molecule of (IV) the oxygen bridge in the C_6–C_2 position is replaced by hydrogen atoms.



The ions with m/e 109, 110, and 111 in (VIII) appear as the result of the detachment of the side-chain nitrogen atom in various combinations with a hydrogen atom from the molecular ion. The intensity of these peaks is only 2–7% of the maximum ion of (VIII)–(IX). In the mass spectra of (VIII) and (IX), as also in (I)–(VI), there are similar peaks with m/e 110 and 111; however, the structures of the ions corresponding to them are different for these substances. The mass spectrum of (IX) differs from that of (VIII) by the high intensity of the peaks, which may be due to the presence of a methyl group on the side-chain nitrogen atom. We have observed this phenomenon in the mass spectrum of (VI). The hydrogen atoms of the methyl group apparently participate in the formation of the fragments with m/e 84 and 85.



The formation of the fragments with m/e 109, 85, and 55 from (IX) is confirmed by the metastable peaks

$$m^+ = 77.5, \text{ for } 154 \rightarrow 109 \text{ calculated } 77.5,$$
$$m^+ = 46.9, \text{ for } 154 \rightarrow 85 \text{ calculated } 46.9,$$
$$m^+ = 36.6, \text{ for } 83 \rightarrow 55 \text{ calculated } 36.6.$$

From goldenchain laburnum (Laburnum angyroides; German "Goldreden") a new alkaloid laburnamine has been isolated [5]; two most probable structural formulas have been proposed for it. On the basis of a comparison of the mass spectra of laburnamine and dihydrodeoxyloline, N-methyldihydrodeoxyloline [2] and some biogenetic considerations, we have concluded that in laburnamine the side-chain nitrogen atom must be at C_1 of the pyrrolizidine nucleus. Consequently, laburnamine must have the structure (X).

(X)

Taking into account all the properties of (I)-(IX) elucidated in mass spectrometry as functions of the positions of the substituting groups, it is easy to propose diagnostic peaks and to give the course of fragmentation of the molecules.

The mass spectra were taken on an MKh-1303 mass spectrometer with an ionizing potential of 31-40 eV, the mass spectra of substances (I), (III), (IV)-(VIII), and (IX) at 150° C and those of (II) and (VII) at 200° C. In the mass spectra of (II), (IV), (V), (VIII), and (IX), all the peaks with the exception of those with m/e 82 and 83 were amplified 2, 1.5, 1.5, 2, and 5 times, respectively.

Conclusions

1. The results of a study of the fragmentation of substances (I)-(IX) under the conditions of mass spectroscopy have confirmed the positions of the side-chain nitrogen atom and the ethereal oxygen.

2. When the functional groups in position C_1 in the molecules of substances (I)-(IX) change, the main fragments remain the same for all the compounds studied and specific fragments appear for each compound.

3. A possible scheme of fragmentation is given for substances (I)-(IX).

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15 May 1967

Institute of the Chemistry of Plant Substances AS UzSSR