FRAGMENTATION OF THE MACROCYCLIC RING OF ALKALOIDS WITH THE OTONECINE NUCLEUS

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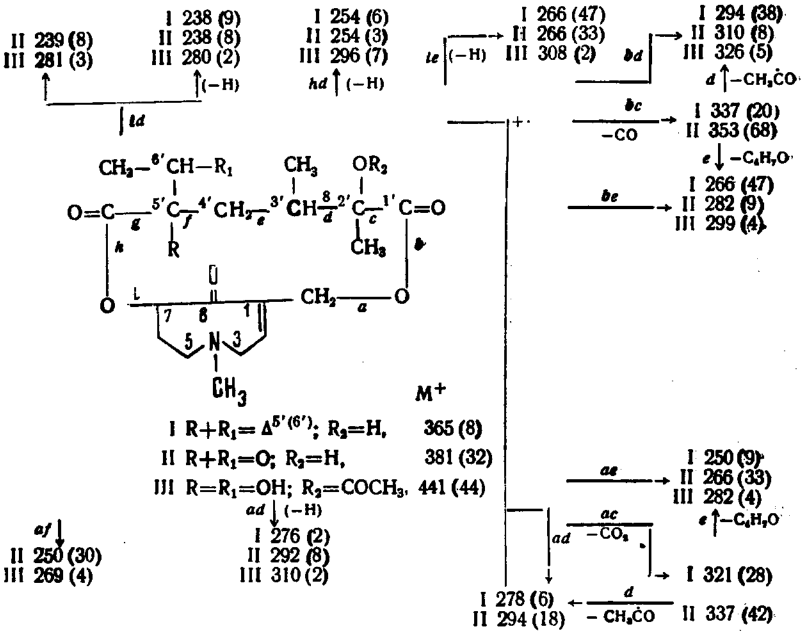
Continuing a study of the mass spectra of pyrrolizidine alkaloids [1, 2], we have studied the decomposition of the macrocycle of bases from plants of the genus Senecio (Compositae): renardine (I) [3], otosenine (II) [4], and floridanine (III) and floricaline (IV) [4, 5].

Characteristic for the otonecine nucleus is a series of ions with m/e 168, 151, 150, 122, 110, and 94, which have been used by several authors [5-8] to establish the assignment of compounds to otonecine diesters; however, here the fragmentation of the macrocyclic ring has not been considered.



Scheme 1

The decomposition of the macrocycles of (I) and (II), differing from one another by an epoxy group in the otosenine molecule (II) at $C_{5'}$-$C_{6'}$, takes place in complex fashion. The corresponding ions in the spectra of (III) and (IV) have very low intensities (Scheme 1).

In the mass spectra of (I) and (II) in the region of high masses, apart from M^+, there are the peaks of the ions $(M-(CH_3))^+$ $(M-OH)^+$, $(M-28)^+$, $(M-44)^+$, and $(M-59)^+$, and in the spectra of (III) and (IV) in addition to the ion $(M-OH)^+$ the ion $(M-H_2O)^+$ appears and the ion $(M-28)^+$ is absent (Fig. 1).

A determination of the elementary compositions of the ions $(M-28)^+$ and $(M-44)^+$ in the spectrum of (II)

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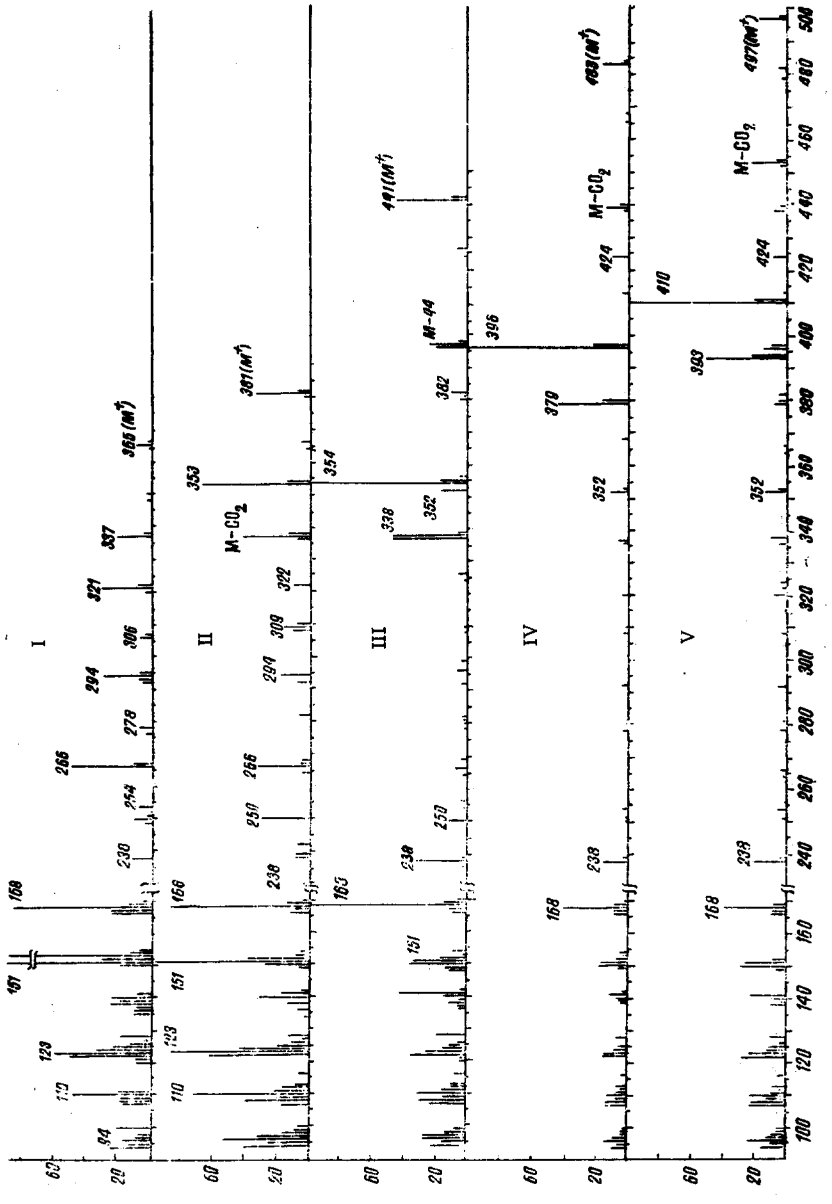

I
II
III
IV
V
60
20
94
110
123
151
167
168
166
165
230
238
250
254
266
278
294
306
309
321
322
337
338
352
353
354
366 (M⁺)
381 (M⁺)
379
382
393
396
410
424
441 (M⁺)
469 (M⁺)
497 (M⁺)
M-CO2
M-44
100
120
140
160
240
260
280
300
320
340
360
380
400
420
440
460
480
500

Fig. 1

TABLE 1. Elementary Compositions of Some of the Ions in the Spectrum of Floridanine III

m/e	Calculated	Found	Composition
441 M^+	441.1998	441.2027	$C_{21}H_{31}O_9N$
397 $M - CO_2$ (a)	397.2100	397.2117	$C_{20}H_{31}O_7N$ (35%)
397 $M-C_2H_4O$ (b)	397.1736	397.1774	$C_{19}H_{27}O_8N$ (65%)
354 M − 87	354.1916	354.1918	$C_{18}H_{28}O_6N$
338 (a) $M -(CO_2 + OCOCH_3)$	338.1968	338.1978	$C_{18}H_{28}O_5N$ (40%)
338 (b) $M - C_2H_4O + OCOCH_3)$	338.1603	338.1614	$C_{17}H_{24}O_6N$ (60%)
238	238.1079	238.1082	$C_{12}H_{16}O_4N$
168	168.1025	168.1024	$C_9H_{14}O_2N$

showed that these fragments are produced by the ejection of molecules of CO and CO_2, respectively. These ions may then decompose by pathways d and e as a result which the radicals $\dot{C}OCH_3$ and C_4H_7O are eliminated (see Scheme 1). Cleavage at the *a*d, *a*e, bd, and be bonds can take place directly in the M^+ ions. Decomposition at ae leads to the formation of ions with m/e 250 (I) and 266 (II), the first of which is analogous in the structure of the side chain to the ion with m/e 220 in the spectrum of senecionine [2].

The $(M - 59)^+$ ions in the spectra of (I) and (II) are formed as a result of a two-stage cleavage reaction, which is confirmed by the detection of the following metastable transitions:

$$\left.\begin{aligned} 268^*=350^+(M-CH_3)^+ &\xrightarrow[-CO_2]{} 306^+ \\ 291.8^*=321^+(M-CO_2)^+ &\xrightarrow[-CH_3]{} 306^+ \end{aligned}\right\} \qquad (I)$$

$$284^*=366^+(M-CH_3)^+ \xrightarrow[-CO_2]{} 322^+ \qquad (II)$$

The $M^+ \rightarrow (M - CO_2)^+ \rightarrow (M - 59)^+$ transition presupposes that the elimination of CO_2 is accompanied by a contraction of the macrocycle.

The appearance of the ion with m/e 250 (250.1085; $C_{13}H_{16}O_4N$) in the spectrum of otosenine (II), the analog of which is absent from the spectrum of (I), is of interest. The peak of this ion is not shifted in the spectrum of the OD analog of (II), i.e., this arises in an af cleavage activated by the oxygen of the epoxide group.

The fragmentation of the ester group at C_7 which we found previously in alkaloids with retronecine and platynecine nuclei appears in the otonecine bases in the form of ions with m/e 238, 254, and 266. The ion with m/e 266 (II) (266.1387, $C_{14}H_{20}O_4N$) of the same composition may arise by two pathways (see Scheme 1). In the structure of their side chain, the ions with m/e 238 and 254 are analogous to the ions with m/e 208 of the spectrum of incanine [1] and with m/e 226 in the spectrum of platyphylline [2], respectively. In the spectrum of (II) there is the peak of an ion with m/e 239. Deuteration showed that it is analogous in the position of cleavage (id) to the ion with m/e 209 in the spectra of trichodesmine [1] and senecionine [2].

The decomposition of the macrocycle of floridanine (III) and floricaline (IV) differs considerably from the decomposition of (I) and (II) in view of the saturated nature of the C_5'-C_6' bond and the presence of an acyloxy group at C_2'. The $(M - 44)^+$ ion is also characteristic for the spectra of (III) and (IV); however, in (III), as a determination of the elementary composition shows, 65% of the $(M - 44)^+$ ions are obtained through the elimination of the substituent at C_5' in the form of acetaldehyde (Table 1 and Scheme 2). The spectrum of (III) also contains an ion $(M - 45)^+$, which can be formed both by the elimination of $CH_3\dot{C}HOH$ from C_5' and of the $\dot{C}OOH$ radical. In the spectrum of (IV), the peak of the $(M - 45)^+$ ion has a low intensity, and the ion produced by the ejection of the radical from C_5' coincides in mass with the ion $(M - 87)^+$ $[(M - CO_2 - CH_3\dot{C}O)^+]$, which is the maximum ion in both spectra (see Fig. 1). In order to establish the nature of the $(M - 45)^+$ ions in the spectrum of (III) and $(M - 87)^+$ in that of floricaline (IV), we synthesized floridanine propionate (V), in the spectrum of which the peaks of the ions under discussion are split.

On calculation it was found that the distribution of the intensities is on an average 3, 12, and 85% for the peaks of the ions $(M - \dot{C}OOH)^+$, $(M - CH_3\dot{C}HOR)^+$ (R = H, $-COCH_3$, $-COC_2H_5$), and $(M - 87)^+$, respectively, of the total intensities of the three ion peaks.

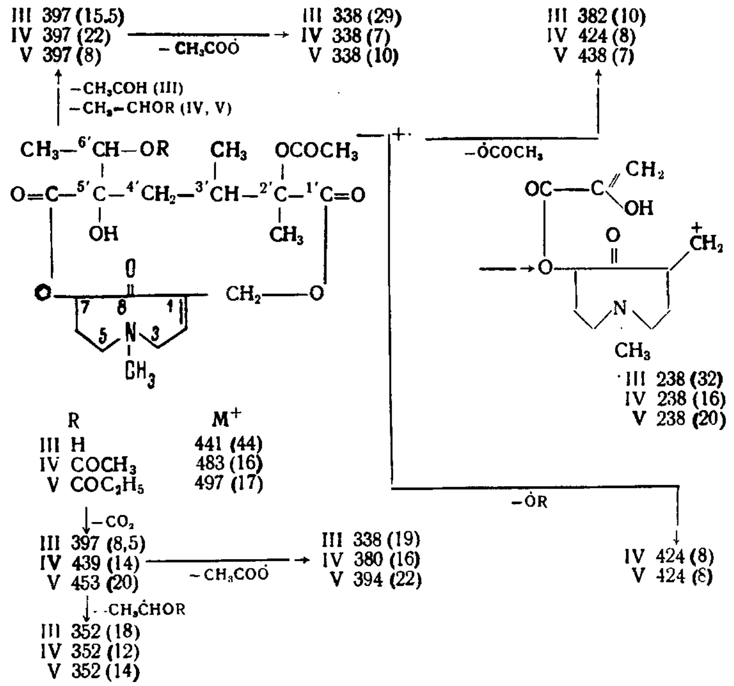
TABLE 2

Compound	Type of cleavage									
	ac	*ad* (+H)	*ad* (−H)	*ae* (+H)	*bc*	*bd* (+H)	*be* (+H)	*ie* (−H)	*id*	*hd* (−H)
Platyphylline	1	3	3	13	0	13	3	3	100	36
Renardine	58	13	4	19	43	60	100	100	19	13
Senecionine	28	25	34	100	2	3	2	2	6	0
Incanine	24	41	16	100	5	5	0	0	30	31

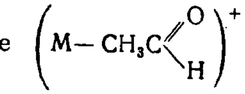
Note. As the 100% peak we took the maximum peak in the region between M^+ and 190 m/e.

In the spectra of (III-V) the peak of an ion with m/e 352 can be seen. Analysis of the spectra of the OD analogs shows that this ion is produced by the elimination of the CH_3CHOR fragment from the ion $(M-CO_2)^+$.

In the region of high masses there are the peaks of ions formed as the result of the ejection of the acyloxy groups, $(M-59)^+$ and $(M-73)^+$, both from C_2' and from C_6' in (IV) and (V). Similar fragments are also eliminated from the $(M-CO_2)^+$ ions, which presupposes the existence of cyclic forms of the $(M-CO_2)^+$ ions. This is confirmed by the formation of an ion with m/e 352.



Scheme 2

The ion with m/e 338 in the spectrum of floridanine (IV) is a doublet: 60% of the ions of this mass arise from the  $\left(M-CH_3C\overset{O}{\underset{H}{\lessdot}}\right)^+$ ions by the ejection of the $CH_3CO\dot{O}$ radical.

The spectra of (III-V) have the peak of an ion with m/e 238 (III); 238.1082, $C_{12}H_{16}O_4N$), which is displaced by 1 amu on deuteration. It is analogous in composition to the ion with m/e 238 in the spectra of renardine (I) and otosenine (II), but this ionis obtained by a multistage decomposition and apparently has the structure shown in Scheme 2.

In view of the mass-spectrometric characteristics of renardine (I), including a senecionic acid residue, it is interesting to compare this spectrum with those of other alkaloids also esterified by this acid (senecionine [9] and platyphylline [9]) which have been characterized previously [2]. This is important from the point of view of estimating the influence of the necine nucleus on the decomposition of the macrocycle (Table 2).

The presence of the $C_1=C_2$ in the senecionine molecule causes an increase in the proportion of cleavages of the *a* bond at the cost of the allyl stabilization of the corresponding cations. In the spectrum of renardine (I), the contribution of these ions decreases, possibly because of the partial delocalization of the π bond through conjugation with $C_8=O$. Simultaneously the contribution of the fragments formed in the cleavage of the b bond increases.

The absence of a π bond in the necine nucleus of platyphylline makes cleavage *a* uncharacteristic, and ions arising in the fragmentation of the ester group at C_7 (id, hd), have the greatest intensities.

An interesting analogy is observed in a comparison of the spectra of senecionine and the 11-membered alkaloid incanine [10], which have the same nucleus and elements of the macrocycle between the *a* and e bonds. The quantitative characteristics of the cleavages of the corresponding bonds are fairly close.

It is known that the CH_3 groups at $C_{2'}$ and $C_{3'}$ in senecionine are in the transoid orientation [11]. On the basis of the results of a study of the mass spectra we have proposed the same mutual orientation for incanine [1]. The similarity of the spectra of these compounds mentioned above confirms this hypothesis.

EXPERIMENTAL

The mass spectra of samples supplied by workers of the alkaloid chemistry laboratory of IKhRV (Institute of the Chemistry of Plant Substances) were taken on an MKh-1303 instrument with a system for the direct introduction of the sample at 110°C with an ionizing voltage of 40 V.

The elementary compositions of the ions were measured on an MS-3301 instrument (Institute of Chemical Physics of the Academy of Sciences of the USSR) with the participation of A. F. Dodonov. The OD analogs were obtained by brief steeping of the samples in CD_3OD.

Floridanine Propionate (V). A solution of 0.13 g of floridanine in a mixture of 1 ml of pyridine and 3 ml of propionic anhydride was kept for 5 days, and then the excess of anhydride and pyridine was evaporated off under vacuum to a volume of 1 ml. The residue was treated with 3 ml of water, neutralized with sodium bicarbonate, and then it was made alkaline with sodium carbonate. Substance (V) was extracted from the mixture with ether (3 × 5 ml). After the elimination of the ether, the residue was recrystallized from acetone. This gave 65 mg of crystals with mp 200-201°C.

SUMMARY

It has been shown that the fragmentation of the macrocycle of the otonecine bases qualitatively resembles the decomposition of macrocyclic alkaloids with the retronecine skeleton. The presence of an oxygen-containing substituent at $C_{5'}$ and of an alkoxy group at $C_{2'}$, when there is no $C_{5'}=C_{6'}$ double bond, substantially changes the direction of decomposition of the macrocycle.

A similarity of the spectra of 11- and 12-membered bases with similar mutual orientation of CH_3 groups at $C_{2'}$ and $C_{3'}$ has been noted.

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