MASS SPECTRA OF N-OXIDES OF PYRROLIZIDINE ALKALOIDS

U. A. Abdullaev, Ya. V. Rashkes,
and S. Yu. Yunusov

UDC 543.51+547.944/945

The mass spectra of saturated heterocyclic N-oxides are characterized by the presence of triplets of peaks of the ions M−16, M−17, and M−18 [1]. It has been established [2] that the appearance of the ion M−16 is due to thermal decomposition. The ease of splitting off of the oxygen atom is obviously in harmony with the oxidizing properties of the N-oxides [3]. With a rise in the temperature, the peak of the M−16 ion rises and that of the M^+ ion falls. When the latter is absent, the triplet of ions mentioned can be used for the identification of the N-oxides. The fragmentary ions present in the spectra of these compounds can be divided provisionally into three main types.

A. Ions, the ancestor of which is the M−16 ion, which practically repeat the peaks of the corresponding free bases.

B. Ions formed from the M−17 and M−18 ions.

C. Ions which, unlike those of series A and B, include the oxygen atom of the N→O group.

It is of particular interest to detect the ions C in the mass spectra of saturated N-oxides, since the nitrogen−oxygen bond in these molecules has a stability close to that of the bond in compounds with a quaternary nitrogen atom not giving the M^+ peaks in the spectra.

We have studied the mass spectra of the N-oxides of a series of pyrrolizidine amino alcohols and esters distributed in the vegetable kingdom in the N-oxide form [3]. The N-oxides of the amino alcohols trachelanthamidine (Ia) [4], oxyheliotridane (Ib), platynecine (Ic), heliotridine (IIa), and retronecine (IIb) [5] show a similar mass-spectroscopic pattern, in the main. The formation of the ions M−17 and M−18 takes place predominantly with the loss of the oxygen atom of the N→O group together with hydrogen atoms from the pyrrolizidine nucleus, as is shown by the results of a study of the spectrum of the OD analog of (Ia) and by the almost complete absence of these peaks in the spectra of the necine alcohols [6].

On the further decomposition of the amino alcohols according to type B, the degree of unsaturation of the nucleus increases. Thus, the ions M−17 and M−18 accompany the ions M−19 and M−20. Adjacent to the main fragments formed by route A there are ions containing one or two less hydrogen atoms. In the N-oxides of amino alcohols with two hydroxy groups (Ic, IIa, IIb) the most highly dehydrogenated ions are observed with m/e 104. The tendency of the N-oxides to undergo dehydration with the subsequent aromatization of the compounds has been observed previously by Yunusov, by a chemical method [3].

Mattocks [7] has given the mass spectra of dehydroretronecine and of dimethoxydehydroretronecine, which were synthesized from the corresponding N-oxides. They contain ions with m/e 104, 106, 117, 118, 135, and 136, corresponding in their masses with the ions of the spectra of (IIa) and (IIb).

The molecular ions in the spectra of (Ia-c) and (IIa, b), have a low intensity. The most stable is the M^+ ion of the N-oxide of trachelanthamidine (Ia). In agreement with this, in its spectrum decomposition of type C is observed: the ion M−30 with m/e 127 (23%).

In the case of the N-oxides of the alkaloids trachelanthamine (Id), viridiflorine (Ie), sarracine (If), echinatine (IIc), heliotrine (IId), trichodesmine (IIIa), and incanine (IIIb) [3], the molecular ion is found

---

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 620-626, September-October, 1974. Original article submitted April 28, 1973.

TABLE 1. Mass Numbers and Relative Intensities (%) of Ions of Types A and B in the Mass Spectra of N-Oxides of Pyrrolizidine Alkaloids

Compound	Nature of C_1-C_2 bond	Substituent at C_7	Substituent at C_1	M^+	M −16	Type A				M −17	M −18	Type B			
I a	C—C	H	α—CH_2OH	157	141	124	83			140	139	122	121	120	108
				33	26	23	100			54	18	20	21	42	50
I b		α—OH	β—CH_3	157	141	97	82			140	139	106	96	95	94
				12	30	72	100			30	65	48	72	32	40
I c		β—OH	β—CH_2OH	173	157	113	82			156	155	137	111	106	96
				0,9	13	26	100			6	24	35	16	48	49
I d		H	α—CH_2O—Trach.	301	285	142	140	124	83	284	283	122	121	120	108
				3	1	30	33	100	54	4	9	35	30	40	21
I e		H	α—CH_2O—Vir.	301	285	142	140	124	83	284	283	122	121	120	103
				2	0,8	23	20	100	29	3	5	24	17	20	17
I f		β—O—Ang.	β—CH_2O—Sar.	353	337	237	222	138	82	336	335	152	136	96	
				—	3	34	27	82	100	0,7	0,7	4,5	24	22	
II a	C=C	α—OH	CH_2OH	171	155	111	80			154	153	136	135	106	104
				0,8	32	76	100			8	57	53	50	35	53
II b		β—OH	CH_2OH	171	155	111	80			154	153	136	135	106	104
				1	35	75	100			10	50	47	38	33	45
II c		α—OH	CH_2O—Vir.	315	299	156	138			298	297	151	136	106	104
				—	5	9	100			0,4	2	21	32	4	6
II d		α—OH	CH_2O—Hel.	329	313	214	197	138		312	311	151	136	106	104
				0,1	2	2	2	84		2	8	21	100	8	5
III a		C_7—β—O—Trich.—OCH_2C_1		369	353	281	264	136	119	352	351	262	135	117	
				—	1	4	9	6	12	0,2	0,6	1	2	42	
III b		C_7—β—O—Inc.—OCH_2—C_1		353	337	292	250	222	119	336	335	204	135	117	
				—	0,7	0,4	0,5	0,9	100	1,4	6	1,4	8	54	
						208	206	136							
						0,3	1,7	11							

Note: Acid Residues: Trach. – trachelanthic; Vir. – viridifloric; Ang. – angelic; Sar. – sarracinic; Hel. – heliotric; Trich. – trichodesmic; Inc. – incanic.

TABLE 2. Calculation of the Spectra of the OD Analogs of (Id) and (Ie) According to Biemann

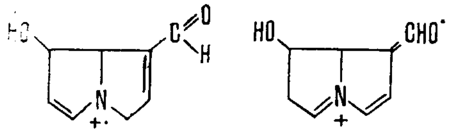
Substance	Ions	Rel. amounts of ions with different numbers of D atoms, %		
		$D=0$	$D=1$	$D=2$
I d	M^+	36	41	23
	M–17, M–18	32	44	24
I e	M^+	53	34	13
	M–17, M–18	52	34	14

TABLE 3. Influence of the Temperature on the Intensities of Some Ions in the Spectrum of (Id)

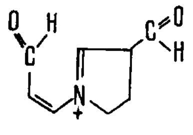
Ion	Temp, °C		
	115	170	225
M − 17	0,51	0,45	0,50
M − 18	0,03	0,13	0,16
M^+	0,36	0,03	0

only in the spectra of (Id, e) and (IId). The triplet of ions M−16, M−17, and M−18 is found in all cases. The results of a calculation of the spectra of the OD analogs by Biemann's method [8] show that the ions M−17 and M−18 are formed by the same mechanism as in the case of the amino alcohol N-oxides, i.e., without the participation of the hydrogen of the OH groups of the side chain. This is indicated by the closeness of the percentages of the shift of the peaks of the ions M^+, M−17, and M−18 in the spectra of the OD analogs (Table 2).

In view of the fact that little attention has been devoted to the origin of the M−18 ion in the literature, we studied the influence of the temperature conditions of the experiment on the relative intensities of a series of ions in the spectrum of the N−oxide of trachelanthamine (Id). Table 3 gives the intensities of the ions M^+, M−16, and M−17 with respect to the intensity of the M−18 ion, taken as unity, at temperatures of the inlet tube of 115°C, 170°C, and 225°C. The sharp decrease in the magnitude of the M^+ peak and the increase in the intensity of M−16 with a rise in the temperature may show the thermal nature of the elimination of the oxygen atom. So far as concerns the M−18 ion, the constancy of the proportion of the intensities of this ion and of the M−17 ion under all conditions shows that the dehydration of the N-oxides takes place predominantly after electron impact. Furthermore, in the spectra of (Id) and (Ie) obtained at 100-115°C we found a m* peak with m/e 266 showing the transition 301 $(M^+) \rightarrow 283$ (M−18). The subsequent splitting off of the substituents at C_1 and C_7 gives rise to ions with m/e 108 (Id, e) and 106, 104 (IIc, d). There are grounds for assuming that the peaks with m/e 151 ($C_8H_9NO_2$) present in the spectra of (IIc, d), together with the m/e 152 ion ($C_8H_{10}NO_2$) in the spectrum of (If) also belong to type B. Their precursor is the M−18 ion, and their most probable structures are as follow:



151 m/e (IIc, IId)



152 m/e (Ie)

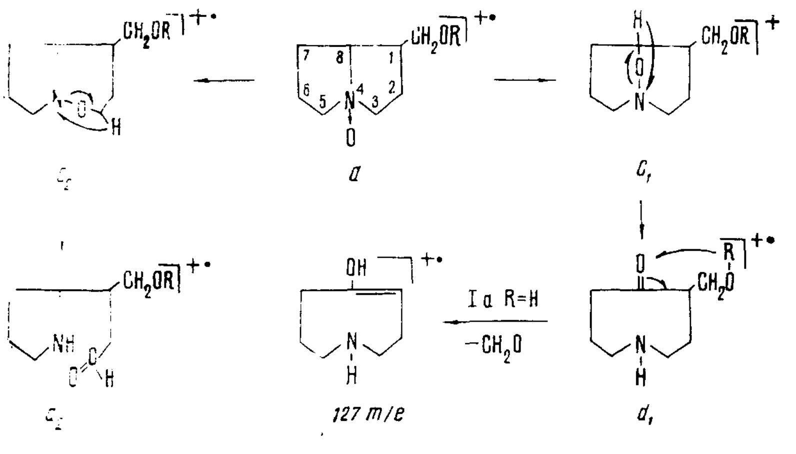
Thus, the ions with m/e 151 are in fact analogous to the M−20 ion in the spectrum of the N-oxide of heliotridine (IIa). The subsequent ejection of OH and CO from the ion with m/e 151 gives an ion with m/e 106, and the elimination of two molecules of CO from the ion with m/e 152 (If) gives an ion with m/e 96.

Ions of type C are observed in the spectra of the N-oxides (Ia) and (Id-f). There is a number of ideas on the question of the mechanism of the retention of the oxygen atom of the N→O group in ions. Schüller [9], having studied the mass spectra of nicotine N-oxide, stated that the N-methylpyrrolidine ring with the N→O group is converted partially into a tetrahydrooxazine ring by thermal rearrangement. Other authors have drawn an analogy between the behavior of N-oxides under the action of electron impact and in their photolysis [10-12]. Thus, fragments are found in the mass spectrum of quinoline N-oxide that belong to one of the photolysis products — 2-quinolone [12].

In spite of the difference in the factors directly responsible for isomerization (heating or electron impact), both ideas start from the assumption of the initial formation of a covalent bond between the N→O oxygen atom and the α-carbon atom of the nitrogen-containing heterocycle.

In the pyrrolizidine N-oxides (Ia) and (Id, f), this transformation can be illustrated in the way shown in Scheme 1.

By analogy with the behavior of the N-oxides of quinoline derivatives, the 1,2-tetrahydrooxazine derivatives C_1 and C_2 may be converted into the oxo derivatives d_1 and d_2. The latter transition, in particular,



Scheme 1

TABLE 4. Elementary Compositions of the Ions in the Spectrum of (IIIa)

m/e	Type of ion	Calc. (C = 12,000000) amu	Found amu	Composition
281	A	281,1627	281,1622	$C_{15}H_{23}O_4N$
264	A	264,1600	264,1601	$C_{15}H_{22}O_3N$
154	SC *	154,0994	154,0982	$C_9H_{14}O_2$
117	B	117,0579	117,0570	C_8H_7N
111 (a)	SC	111,0810	111,0802	$C_7H_{11}O$ (80%)
111 (b)	SC	111,0446	111,0445	$C_6H_7O_2$ (20%)

* SC — side chain.

is responsible for the appearance of an ion M−30 in the spectrum of (Ia) by the ejection of a molecule of formaldehyde from d_1 through a six-membered state with the transfer of the hydrogen of the OH group to the oxygen of the $C_8=O$ group.

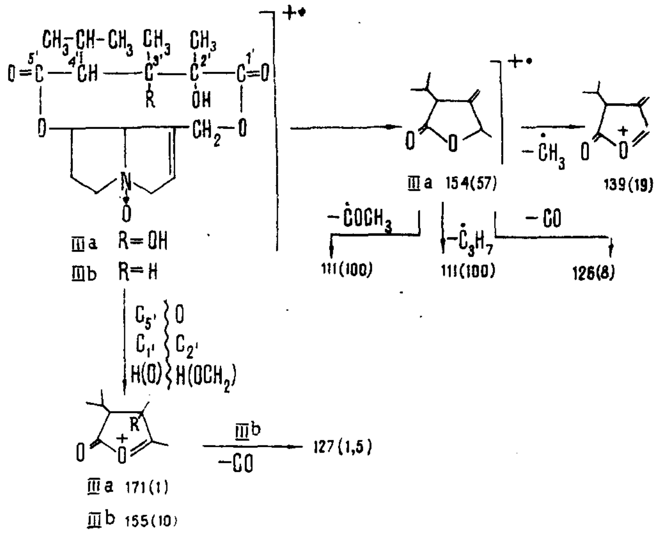
The ions of type C in the spectra of the alkaloids (Id-f) are the products of the fragmentation of the side chain, which contains an additional oxygen atom. These ions are also, apparently, present in the form of oxazines or oxo amines. Below we give the mass numbers and intensities (%) of the type C ions:

Id	m/e	258	257	256	158	156	140
	I	7	13	42	57	36	33
Ie	m/e	258	257	256	158	156	140
	I	3	11	24	31	20	20
If	m/e	253	(M − Ang. − OH)$^+$				
	I	3,5					

In the spectra of the N-oxides (IIa-d) and (IIIa, b) the type C ions are absent, which is explained by the greater tendency to decomposition of types A and, particularly, B activated by the $C_1=C_2$ π bond. The ions with m/e 117, 118, 134, and 135 in the spectrum of dehydromonocrotaline [7] correspond to the type B ions (IIIb) and (IIIa). The ion with m/e 262 of the latter is analogous to the ion with m/e 234 of dehydromonocrotaline. The composition of the ion with m/e 117 (C_8H_7N) is confirmed by the results of its measurement on a high-resolution instrument (Table 4).

In the spectra of the N-oxides of alkaloids there is also a series of intense fragments formed by the localization of the charge in the side chain. Their proportion in the total ion current rises in view of the fact that the N→O oxygen leads to a decrease in the number of ions with the localization of the charge on the nitrogen atom. Thus, in the spectra of the N-oxides of echinatine and heliotrine (IId) the intensities of the ions with m/e 117 and 131, having the structure of the acid residues of viridifloric and heliotrinic acids, respectively, rise [13].

The most interesting results were obtained in an analysis of the spectra of the N-oxides (IIIa) and (IIIb), which contain intense fragments with m/e 154, 139, and 111, especially (IIIa). The results of measurements of the elementary compositions of the ions with m/e 154 and 111 (see Table 4) on a high-resolution instrument have shown that they contain no nitrogen atom and, consequently, are formed through the macrocyclic ring. The most probable route for the formation of these and some other ions is shown below.



The spectrum of the N-oxide of incanine (IIIb) contains an ion with m/e 155 having the composition $C_9H_{15}O_2$. It can be seen from the subsequent decomposition of the ion with m/e 154 that it probably has the structure of a dehydrated deacyl cation of a lactone acid. The ion with m/e 111 corresponds to a doublet, the more intensive component of which is formed by the ejection of a CH_3CO fragment and the less intensive by the detachment of an isopropyl radical from the ion with m/e 154.

Experimental conditions: MKh-1303 instrument, temperature 100-120°C, ionizing voltage 40V. The N-oxides of the amino alcohols (Ia), (Ib), (Ic), (IIa), and (IIb), of which (Ib) (mp 104°C) has not been described previously, were obtained by the usual method [14], and the OD analogs by dissolving the samples in CD_3OD followed by the pumping off of the solvent in the lock system of the mass spectrometer. The elementary compositions of the ions were measured on a MS-3301 instrument (Institute of Chemical Physics of the Academy of Sciences of the USSR) with the participation of A. F. Dodonov.

SUMMARY

The mass spectra of the N-oxides of pyrrolizidine alkaloids show three main types of ions formed as the result of the detachment of the oxygen of the N → O group, dehydration with subsequent dehydrogenation, and isomerization of the nucleus. In a number of spectra the proportion of ions formed by the localization of the charge in the side chain increases.

LITERATURE CITED

1. N. Bild and M. Hesse, Helv. Chim. Acta, 50, 1885 (1967).
2. A. M. Duffield and O. Buchardt, Acta Chem. Scand., 26, 2423 (1972).
3. S. Yu. Yunusov, Alkaloids [in Russian], Tashkent (1968); S. Yu. Yunusov, Tr. In-ta Khimii, Tashkent, 16 (1952).
4. G. P. Men'shikov and G. M. Borodina, Zh. Obshch. Khim., 11, 209 (1941).
5. H. G. Boit, Ergebnisse der Alkaloid-Chemie bis 1960, Akademie Verlag, Berlin (1961), p. 99.
6. N. Neuner-Jehle, H. Nesvadba, and G. Spitelier, Monatsh., 96, 321 (1965).
7. A. R. Mattocks, J. Chem. Soc., C, 1155 (1969).
8. K. Biemann, Mass Spectrometry, McGraw-Hill, New York (1962), p. 223.
9. D. Schüller and H.-P. Harke, Org. Mass Spectrom., 7, 839 (1972).
10. G. G. Spense, E. C. Taylor, and O. Buchardt, Chem. Rev., 70, 231 (1970).
11. J. H. Bowie, R. G. Cooks, N. C. Jamieson, and G. E. Lewis, Austr. J. Chem., 20, 2545 (1967).
12. O. Buchardt, A. M. Duffield, and R. H. Shapiro, Tetrahedron, 24, 3139 (1968).
13. U. A. Abdullaev, Ya. V. Rashkes, Kh. Shakhidoyatov, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 634 (1972).
14. L. Fieser and M. Fieser, Organic Chemistry, 3rd ed., Van Nostrand-Reinhold, New York/Chapman and Hall, London (1956).