FEATURES OF THE MASS SPECTRA OF C_{18}-DITERPENE ALKALOIDS

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Fragmentation under electron impact of eleven C_{18}-diterpene alkaloids with an oxygen function at C-4 has been investigated. The contributions of various modes of forming the $(M - CH_3)^+$ ions have been determined. The mechanism of the appearance of the fragments $(M - CH_3)^+$ and $(M - OCH_3)^+$ at the expense of the methoxy groups at C-14 and C-16 has been considered. The characteristic nature of the parameters of the metastable peaks in the transitions to these daughter ions has been shown. Minor directions of the fragmentation of 3,4-epoxy- and 4-hydroxy bases have been characterized.

C_{18}-Diterpene alkaloids are found in several species of plants of the genera Aconitum and Delphinium [1]. With the exception of aconosine [2], they all contain an oxygen function at C-4. This group of compounds also contains the 3,4-epoxy bases monticamine (I) [3], monticoline (II) [3], and excelsine (III) [4] and their corresponding dihydro derivatives: dihydromonticamine (IV) [5], dihydromonticoline (V) [3], and lappaconidine (VI) [6].

In general form, the mass spectra of (I)-(VI) have been characterized previously [7, 8]. In [7] there is a suggestion that the redistribution of the intensities of the peaks of the $(M - CH_3)^+$ and $(M - OH)^+$ ions in the spectra of bases (I-III) is due to the presence of a 3,4-epoxy group. This was confirmed indirectly by the spectra of the dihydro bases (IV-VI), repeating the main features of the spectra of the C_{19} lycoctonine alkaloids.

The source of the appearance of the 100% peaks of the $(M - CH_3)^+$ ions in the spectra of (I-III) has not been established. The processes involved in the appearance of the peak of the $(M - 31)^+$ ion, second in intensity, in the spectra of monticamine (I) and of excelsine (III) have not been considered. Subsidiary fragmentation pathways of compounds (I-VI) have not been characterized in detail. These questions have been made the object of discussion in the present paper.

An analysis of the metastable transitions $M^+ \rightarrow (M - 15)^+$ in compounds (I-III) [7] indicated that the processes for the formation of this daughter ion were monotypical, but no concrete "reacting elements of the structure" (RESs) were determined. In addition to the most probable process for the splitting out of $\dot{C}H_3$ from the N-ethyl group, the detachment of a methyl radical from the methoxy groups at C-14 and C-16 can serve as source of appearance of the $(M - CH_3)^+$ ions. In view of this, we have studied the mass spectra of N-normonticamine (VII) and the d_5 analog of monticamine obtained from it (VIII). In addition to this, attempts have been made to obtain O-demethylated products from compounds (I) and (II) in reactions with $(CH_3)_3SiCl + NaI$, which would also lead to an answer to the question of the source of ejection of methoxy groups. However, this reaction led to Δ^2-dihydromonticamine (IX) and Δ^2-dihydromonticoline (X), isomeric with the initial bases, and to the corresponding 3-iododihydro derivatives. A similar type of isomerization of 3,4-epoxy bases has been observed under the action of 10% H_2SO_4 [9].

The mass numbers, relative intensities, and elementary compositions of the fragments are given in Table 1.

On passing from monticamine (I) to N-normonticamine (VII) the stability of the molecular ion W_{M^+} increased 1.5-fold, while the stability of the $(M - 15)^+$ ion decreased almost 4-fold. This indicates the predominant formation of the $(M - 15)^+$ ion of monticamine through the splitting out of a methyl radical from the N-ethyl group. It is possible to

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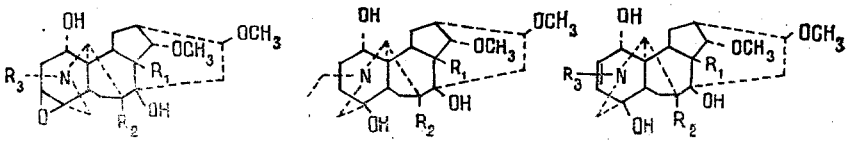
TABLE 1. Mass Numbers (m/z), Relative Intensities (%), and Elementary Compositions of the Main Fragments in the Mass Spectra of Compounds (I-IX)



I–III, VII, VIII IV–VI IX–XI

I. R_1, R_2, =H; R_3=C_2H_5
II. R_1=H; R_2=OH; R_3=C_2H_5
III. R_1=OH; R_2=H; R_3=C_2H_5
VII. R_1, R_2, R_3=H
VIII. R_1, R_2=H; R_3=C_2D_5
IV. R_1, R_2=H
V. R_1=H; R_2=OH
VI. R_1=OH; R_2=H
IX. R_1, R_2=H; R_3=C_2H_5
X. R_1=H; R_2=OH; R_3=C_2H_5
XI. R_1, R_2=H; R_3=C_2D_5

I 391 (M^+, $C_{22}H_{33}NO_5$; 41), 376 (100), 374 (17), 363 ($C_{21}H_{33}NO_4$; 6), 363 ($C_{20}H_{29}NO_5$; 2), 362 ($C_{21}H_{32}NO_4$; 7), 360 ($C_{21}H_{30}NO_4$; 70) 358 ($C_{21}H_{28}NO_4$; 9), 348 ($C_{20}H_{30}NO_4$; 21), 346 (6), 344 ($C_{21}H_{30}NO_3$; 4), 344 ($C_{20}H_{26}NO_4$; 3), 342 ($C_{21}H_{28}NO_3$; 9), 336 ($C_{19}H_{30}NO_4$; 8), 332 ($C_{19}H_{26}NO_4$; 6), 332 ($C_{20}H_{30}NO_3$; 2), 330 ($C_{20}H_{28}NO_3$; 8), 328 (4) 326 (4), 324 ($C_{21}H_{26}NO_2$; 5); 320 ($C_{18}H_{26}NO_4$; 1), 320 ($C_{19}H_{30}NO_3$; 3), 305 ($C_{18}H_{25}O_4$; 5), 304 ($C_{19}H_{30}NO_2$; 1), 304 ($C_{18}H_{26}NO_3$; 3,3), 302 ($C_{18}H_{24}NO_3$; 3), 302 ($C_{19}H_{28}NO_2$; 3), 300 (4), 272 ($C_{17}H_{22}NO_2$; 6), 232 ($C_{15}H_{20}O_2$; 9); 208 ($C_{12}H_{18}NO_2$; 8), 190 ($C_{12}H_{16}NO$; 11), 190 ($C_{11}H_{12}NO_2$; 3); 112 (13), 98 (12), 84 (25), 58 (35).

II 407 (M^+, $C_{22}H_{33}NO_6$; 35). 392 ($C_{21}H_{30}NO_6$; 100), 390 ($C_{22}H_{32}NO_5$; 6), 379 (2), 378 (3), 376 ($C_{21}H_{30}NO_5$; 11), 374 (10), 364 ($C_{20}H_{30}NO_5$; 9), 360 ($C_{21}H_{30}NO_4$; 4), 360 ($C_{20}H_{26}NO_5$; 4), 358 ($C_{21}H_{28}NO_4$; 7); 348 (2), 346 ($C_{20}H_{28}NO_4$; 6), 344 (4), 342 (2), 336 (3), 334 (3), 332 (2), 330 (4), 328 (3), 321 (2), 320 (2), 318 (3), 317 ($C_{19}H_{25}O_4$; 3), 316 (3), 314 (3), 306 ($C_{18}H_{28}NO_3$; 4), 305 (2), 304 (2), 302 (4), 300 (2), 288 (2), 286 (3), 274 ($C_{16}H_{20}NO_3$; 1), 274 ($C_{17}H_{24}NO_2$; 2), 248 ($C_{15}H_{20}O_3$; 6), 244 ($C_{15}H_{16}O_3$; 5), 232 ($C_{14}H_{18}NO_2$ 4), 222 ($C_{12}H_{16}NO_3$; 5), 112 (15), 98 (6), 84 (6), 58 (22).

III 407 (M^+, $C_{22}H_{33}NO_6$; 58), 392 (100), 390 (18), 379 (12), 378 (8), 376 ($C_{21}H_{30}NO_5$; 96), 374 (10), 364 (28), 358 (16), 352 (8), 348 (10), 346 (8), 336 (9), 330 (8), 321 ($C_{18}H_{25}O_5$; 19), 318 (9), 304 (5), 302 (4) 288 ($C_{17}H_{22}NO_3$; 7), 248 (2), 208 ($C_{12}H_{18}NO_2$; 11), 206 ($C_{12}H_{16}NO_2$; 9), 190 ($C_{12}H_{15}NO$; 9), 190 ($C_{11}H_{12}NO_2$; 2), 112 (14), 98 (8), 84 ($C_5H_{10}N$; 22), 58 (C_3H_8N; 23).

IV 393 (M^+ $C_{22}H_{35}NO_5$; 41), 378 (33), 376 (100), 364 (2), 362 (3), 360 (16), 350 (1), 344 (2), 337 ($C_{19}H_{31}NO_4$; 15), 335 ($C_{19}H_{29}NO_4$; 1), 322 ($C_{18}H_{28}NO_4$; 6), 319 (1), 304 ($C_{18}H_{26}NO_3$; 1), 276 ($C_{17}H_{24}O_3$; 2), 276 ($C_{17}H_{26}NO_2$; 1), 275 ($C_{17}H_{23}O_3$; 2), 244 (1), 242 (1), 98 (3), 84 (5), 58 (6).

V 409 (M^+, $C_{22}H_{35}NO_6$; 20), 394 (68), 392 (100), 378 (7), 376 (24), 374 (3), 366 (6), 362 (3), 360 (12), 353 ($C_{19}H_{21}NO_5$; 8), 351 ($C_{19}H_{29}NO_5$; 1), 338 ($C_{18}H_{28}NO_5$; 10), 292 ($C_{17}H_{24}O_4$; 1), 292 ($C_{17}H_{26}NO_3$; 1), 291 ($C_{17}H_{23}O_4$; 3), 242 (2), 98 ($C_6H_{12}N$; 1), 98 (C_5H_8NO; 2), 84 (9), 58 (8).

VI 409 (M^+, $C_{22}H_{35}NO_6$; 43), 394 (33), 392 (100), 378 (4), 376 (20), 374 (1), 366 (1), 364 (1), 363 ($C_{20}H_{29}NO_5$ 1), 362 ($C_{21}H_{32}NO_4$; 1), 362 ($C_{20}H_{28}NO_5$; 1), 360 (3), 353 (15), 351 (3), 348 (2), 338 ($C_{18}H_{28}NO_5$; 10), 324 ($C_{18}H_{20}NO_4$; 1), 322 ($C_{18}H_{28}NO_4$; 1), 310 ($C_{17}H_{28}NO_4$; 1), 304 ($C_{18}H_{26}NO_3$; 1), 302 ($C_{18}H_{24}NO_3$; 1), 292 ($C_{17}H_{24}O_4$; 1), 291 ($C_{17}H_{23}O_4$; 4), 93 (3), 84 (3), 58 (4).

VII 363 (M^+, $C_{20}H_{29}NO_5$; 100), 348 (40), 346 (16), 345 (66), 335 (22), 334 (34), 332 (49), 330 (40), 320 (26), 318 (12), 316 (16), 314 (38), 308 (12), 304 (9), 302 (21), 300 (10), 298 (14), 296 (25), 286 (16), 162 (32), 58 (10).

TABLE 1 (continued)

VIII 396 (M^+, $C_{22}H_{28}D_5NO_5$; 90), 381 (45), 379 (25), 378 ($C_{21}H_{28}D_2NO_5$; 100), 378 ($C_{22}H_{26}D_5NO_4$; 7), 368 (9), 367 (8), 365 (93), 353 (12), 351 (7), 350 (22), 347 (12), 341 (11), 337 (11), 335 (10), 324 (13), 309 (7), 306 ($C_{18}H_{24}DO_4$; 11), 232 ($C_{15}H_{20}O_2$; 12), 213 ($C_{12}H_{13}D_5NO_2$; 17), 195 ($C_{12}H_{11}D_5NO$; 17), 117 ($C_6H_5D_5NO$; 18), 103 (8), 89 (19), 63 (38).

IX 301 (M^+, $C_{22}H_{33}NO_5$; 8), 376 (100), 374 (9), 360 (11), 358 (8), 348 (2), 346 (2), 345 (2), 344 (2), 342 (3), 330 (2), 328 (2), 326 (2), 318 (1), 316 (1), 314 (1), 312 (1), 302 (1), 300 (1), 298 (2), 112 (3), 98 (3), 84 (7), 58 (9).

X 407 (M^+, $C_{22}H_{33}NO_6$; 15), 392 (100), 390 (6), 376 (6), 374 (8), 358 (3), 346 (1), 342 (1), 330 (1), 328 (1), 326 (1), 314 (1), 300 (1), 112 (4), 98 (5), 84 (6), 58 (8).

XI 396 (M^+, $C_{22}H_{28}D_5NO_5$; 37), 381 (77), 378 (100), 365 (14), 363 (16), 353 (17), 351 (15), 350 (19), 341 (7), 340 (12), 285 (12), 89 (27), 63 (66).

arrive at the same conclusion in an analysis of the spectrum of the d_5 analog of (VIII): the heights of the peaks of the $(M - CH_3)^+$ and $(M - CD_3)^+$ ions are in a ratio of 5:11. To answer the question of the contributions of the two processes for the splitting out of CH_3 in the fragmentation of other 3,4-epoxy bases let us consider the parameters of the corresponding metastable transitions obtained by the method of defocussing the ion beam in the first field-free space of the mass spectrometer (MD). Repeated measurement of the relative intensities of the metastable peaks (the magnitudes A [7]) in the transitions $M^+ \rightarrow (M - 15)^+$ of the epoxy bases (I-III) gave values of 7.6-13.6%, which agrees completely with the figures obtained previously [7] (Table 2). A criterion of the monotypicity of the fragmentation reactions is the close values of the A/Σ_d ratios [7, 10] (where Σ_d is the contribution of the daughter ion to the total ion current).

For the epoxy bases (I-III), these values are close, amounting to 0.41-0.50 (average 0.44) and differ substantially from the analogous values for the dihydro bases (IV-VI) [7]. However, the intensities of the metastable peaks do not always reflect the nature of the fragmentation process. It is considered that the form of the peaks correlates to a greater degree with the structure of the parental and daughter ions [11]. As has now been established, the energy of the metastable transition (T), in the calculation of which use was made of the energy width of the metastable peak at some particular height of it [12], characterizes the change in the mechanism of the splitting out of a fragment fairly reliably. Thus, the average value of T for the metastable transition $M^+ \rightarrow (M - 15)^+$ in the spectra of 10 bases splitting out methyl radicals predominantly from the C_6–OCH_3 group was 1.7 times higher than the analogous magnitude in the spectra of nine lycoctonine bases splitting out $\dot{C}H_3$ mainly from the N-ethyl group [10]. Thus, the rise in the value of T showed a difference between the central cleavage of the bond in N–Et and the more complex process of the ejection of $\dot{C}H_3$ from C_6–OCH_3 taking place by the breakdown of not less than two bonds.

Let us consider the value of T for the $M^+ \rightarrow (M - 15)^+$ of the epoxy bases from this point of view. For compounds (I-III) they fall into the narrow interval of 3.24-3.48 eV (see Table 2) and are intermediate between the values T = 4.91 and 2.72 eV for the $M^+ \rightarrow (M - CH_3)^+$ and $M^+ \rightarrow (M - CD_3)^+$ transitions in the spectrum of the d_5 analog (VIII). The first of the values of T confirms the complex nature of the formation of the $(M - CH_3)^+$ ions in comparison with the simple cleavage of a C–C bond in the N–Et groups. The value of T for the $M^+ \rightarrow (M - CH_3)^+$ transition in the spectrum of N-normonticamine (VII) agreed well with the analogous value in the spectrum of the d_5 analog (VIII). It follows from all that has been said above that the ratio between the contributions of the ejections of $\dot{C}H_3$ from the N–Et and O–Me groups in monticoline and excelsine are of the same order as in monticamine.

TABLE 2. Values of T and A for the Metastable Transitions $M^+ \rightarrow (M - CH_3)^+$ and $M^+ \rightarrow (M - OCH_3)^+$ in the MD Spectra of Compounds (I-III) and (VII-XI)

Compound	$M^+ \rightarrow (M-CH_3)^+$						$M^+ \rightarrow (M-OCH_3)^+$			
	ΔW	T, eV	$\Delta W_{0,5}$	$T_{0,5}$, eV	A	A/Σ_d	ΔW	T, eV	A	A/Σ_d
I	75,2	3,30	52,8	1,60	8,9	0,50	91,1	2,02	2,8	0,17
II	72,0	3,24	51,4	1,66	13,6	0,42	92,6	2,21	0,33	0,13
III	75,9	3,48	52,6	1,67	7,6	0,41	85,0	1,89	3,6	0,23
VII	94,1	4,69	57,9	1,80	—	—	94,5	1,99	1,5	0,21
VIII	$(-\dot{C}H_3)$ 82,0	4,91	49,2	1,77	—	—	93,4	2,16	2,6	0,17
	$(-\dot{C}D_3)$ 63,2	2,72	50,4	1,48						
IX	89,9	4,67	52,3	1,53	37,3	0,73	95,8	2,24	2,8	0,50
X	81,6	4,20	50,2	1,58	40,5	0,85	95,6	2,34	2,0	0,31
XI	$(-\dot{C}H_3)$ 98,0	5,62	55,3	1,79	—	—	96,1	2,29	2,6	0,42
	$(-\dot{C}D_3)$ 75,7	2,72	53,4	1,35						

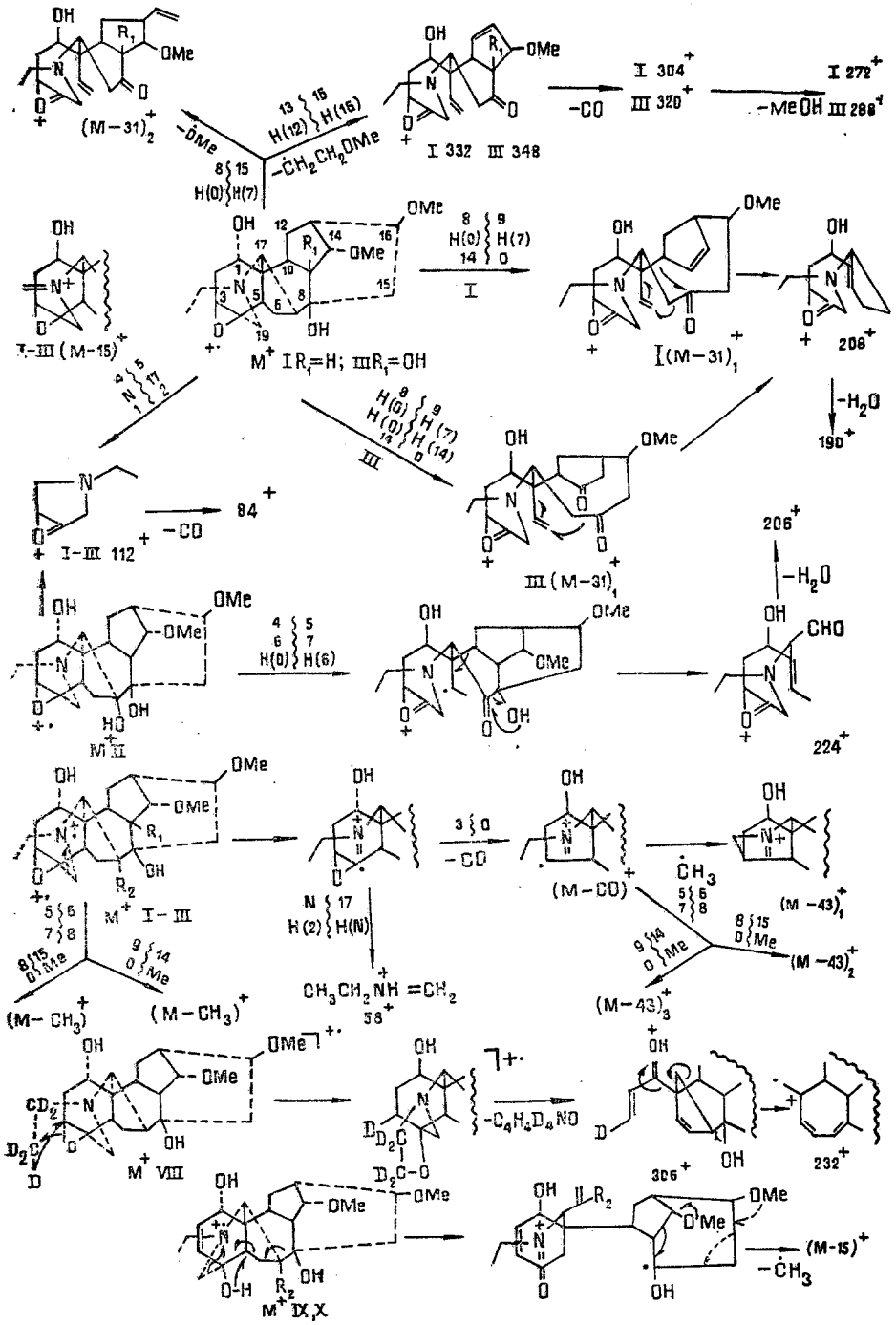
Let us now consider the spectra of the Δ^2-derivatives (IX) and (X) isomeric with monticamine and monticoline. The stability of their molecular ions is little more than half that for (I) and (II). At the same time, the selectivity of fragmentation has risen in favor of the splitting out of $\dot{C}H_3$. The stability $S_{(M-15)^+}$ amounts to 51.0% for (IX) and 66.5% for (X). The contribution of the $(M - 31)^+$ ion in the monticamine isomer as compared with the initial base (I) has fallen almost 3-fold, while for Δ^2-dihydromonticamine it has remained at the same level as in (II). This relates to the processes for the splitting out of radicals from C-1 that are the main ones for the dihydro derivative (IV)-(VI) just as for the majority of other diterpene alkaloids [13, 14], while in the spectra of (IX) and (X) they have secondary importance in spite of the presence of a π-bond in the colchicine α,β-position which, it would appear, should intensify fragmentation in this direction. This can be explained by the existence of an alternative fragmentation mechanism based on the initial cleavage of the C-4–C-19 bond, the tendency to which is raised because of the Δ^2-bond.

Here we observe an analogy with the behavior of the EI of the lycoctonine alkaloids with a $\Delta^{10(12)}$-bond [15]: the cleavage of the C-11–C-17 bond in these compounds, just like the cleavage of the C-4–C-19 bond in the molecular ions (IX) and (X) under consideration leads to the delocalization of the π-bond and to the stabilization of the corresponding form of the molecular ions. Thereby the contribution of the process in which the substituent is split out from C-1 decreases. Literature information on the characteristic ions of Δ^2-bases – ibukinamine [16], tatsiensine, and deacetyltatsiensine [17] – also indicates a sharp decrease in the intensity of the peaks of the $(M - OR_1)^+$ ions.

The values of A, A/Σ_d and T for the transition $M^+ \rightarrow (M - 15)^+$ in the spectra of (IX) and (X) are appreciably raised in comparison with the corresponding values for the epoxy bases (I) and (II) (see Table 2). In order to explain the reason for this phenomenon, we have obtained the d_5-analog of Δ^2-dihydromonticamine (XI). In its spectrum, the heights of the peaks of the $(M - CH_3)^+$ and $(M - CD_3)^+$ ions are in a ratio of 3:4;, i.e., the proportion of $(M - CH_3)^+$ ions here is considerably higher than in the spectrum of monticamine-d_5 (VIII). The value of T for the $M^+ \rightarrow (M\text{-}CD_3)^+$ transition equals 2.72 eV and coincides with like non-isomerized d_5-analog (VIII). Thus, the mechanisms of the breakdown of the N-ethyl group of isomers (I) and (IX) are monotypical, and the structure of ring A has no appreciable effect on them. Conversely, T for the $M^+ \rightarrow (M - CH_3)^+$ transition (5.62 eV) is considerably higher than in the analogous process for monticamine-d_5. Both factors – the rise in T and the increase in the contribution of this process to the total ion current – lead to an increase in the total T in the spectra of (IX) and (X) (4.67 and 4.20 eV, respectively). The reasons for the change in T will be considered in a discussion of fragmentation schemes (see scheme on following page).

The measurements of the energies of the metastable transitions at the levels of the half-height of the metastable peak ($T_{0,5}$; see Table 2) then performed showed that these magnitudes were less sensitive to the structure of the individual compounds but were not less characteristic in relation to the methods of formation of the $(M - CH_3)^+$ ions. Thus, the values of $T_{0,5}$ of the transition $M^+ \rightarrow (M - CH_3)^+$ for the isomeric compounds (VIII) and

(XI) were very close to one another (1.77 and 1.79 eV). The splitting out of $\dot{C}D_3$ gave, as an average, $T_{0.5}$ = 1.42 eV (cleavage of a single bond). The splitting out of $\dot{C}H_3$ showed, as an average, the substantially greater value of 1.79 eV (cleavage of several bonds). The values of $T_{0.5}$ for the nondeuterated compounds were at the intermediate level of 1.58-1.67 eV because of the superposition of not less than two methods of elimination of the methyl radical.



Scheme 1. Fragmentation of the 3,4-epoxy bases (I-III, VIII) and of the Δ^2-dihydrobases (IX, X).

Let us now discuss the most probable mechanisms for the fragmentation of the methoxy groups taking place with the formation of the $(M - 15)^+$ and $(M - 31)^+$ ions in the spectra of the epoxy compounds (I-III, VII). It is obvious that the increase in the contribution of these processes is due to the suppression of competition on the part of the process in which the substituent is split out from C-1. Since the latter is initiated by the cleavage of the C-11–C-17 bond, different initial acts must be realized in the molecular ions of the epoxy bases. They are, in the first place, the cleavage of the bonds adjacent to the epoxide unit – C-4–C-19, with the localization of the charge on the nitrogen atom, and C-4–C-5, with the positive charge present on the oxygen atom of the epoxy group. The possibility of the localization of the charge on the oxygen atoms of the heterocycles included in the molecules of the bases has also been shown in other studies [18], including some on the fragmentation of diterpene alkaloids [15]. The cleavage of the C-4–C-19 bond is accompanied by the breakage of bonds in rings B, C, and D and leads to different types of $(M - CH_3)^+$ ions (Scheme 1). A second method of initiation causes a different series of cleavages, as a result of which two types of $(M - OCH_3)^+$ ions arise with the splitting out of methoxyl from C-14 $(M - 31)_1^+$ and from C-16 $(M - 31)_2^+$ (Scheme 1). The first type of ions then breaks down with the formation of fragments having m/z 208 ($C_{12}H_{18}NO_2$), as is confirmed by the MD spectra (a list of transitions revealed by the MD method is given in Table 3). The m/z 208 ions, including a molecule of water, are converted into m/z 190 ions. In the spectrum of the d_5-analog (VIII) both these ions are shifted in the direction of higher mass numbers by 5 m.u. In the spectrum of N-normonticamine (VII) an analogous ion with m/z 180 (162 a.m.u.) can be seen.

The $(M - 59)^+$ ions in the spectra of (I) and (III) consist of the components $(M - CO - OCH_3)^+$ and $(M - C_3H_7O)^+$. The second can be represented as the product of the splitting out of the elements of ring D as the result of C-8–C-15 and C-13–C-16 cleavages (Scheme 1). The ions with m/z 332 (I) and 348 (III) formed in this way then break down with the splitting out of CO and MeOH or CH_2O.

The hypothesis of the localization of the charge on the epoxide oxygen atom helps to explain the reason for the decrease in the contribution of the $(M - 31)^+$ ions in the spectrum of monticoline (II). The C-4–C-5 and C-6–C-7 cleavages are followed by an act of the migration of the C_7–OH hydrogen to C-6, which prevents the C-8–C-9 and C-8–C-15 cleavages initiating the splitting out of OMe. Instead of this process, the intermediate structure M^+ (II) tends to break down at the C-10–C-11 and C-7–C-8 bond, which leads to an ion with m/z 224 that loses water with the formation of an ion with m/z 306 (see Scheme 1). It must be observed that the explanation given above of the reason for the redistribution of the contributions of the main fragments in the spectrum of the 7,8-diol monticoline cannot be extended to other 7,8-diols in the spectra of which a similar phenomenon is observed [8].

In spite of the difference in the contributions of the processes forming the $(M - 31)^+$ ions in various epoxy bases and the probability of the participation of either of the two methoxyls in this process, the values of T for the $M^+ \rightarrow (M - 31)^+$ transition (see Table 2) range within fairly narrow limits and average 2.05 eV. The corresponding ratios A/Σ_d likewise change little. The energies of the same transitions in the case of the Δ^2-bases (IX) and (X) are appreciably greater (2.24 and 2.34 eV), which reflects the difference in the structures in the $(M - 31)^+$ ions of the isomeric compounds.

Pelletier et al. [19] gives a list of the main fragments in the spectrum of 6-methoxymonticoline – tuguaconitine. Together with the 100% peak of the $(M - 15)^+$ ion it is possible to see an increased intensity of the peak of the $(M - 31)^+$ ion (40%) and to regard this fact as a consequence of an initial C-4–C-5 cleavage followed by the splitting out of methoxyl from C-6. There is no doubt that some of the $(M - 15)^+$ ions in this spectrum arise on the splitting out of $\dot{C}H_3$ from the same substituent.

Among the fragments of the spectra of the epoxy bases (I-III) treated from the point of view of the localization of the charge on the nitrogen atom, in addition to the $(M - 15)^+$ ions at the expense of the N-ethyl group must include the m/z 58 (C_3H_8N) ions. A combination of α- and N–C-cleavages with the migration of hydrogen to the nitrogen atom that is typical for tertiary amines leads to their appearance. The same initial act leads to a rearrangement in ring A with the elimination of a CO molecule (see Scheme 1). The $(M - CO)^+$ ions are stabilized by the splitting out of $\dot{C}H_3$ and the formation of $(M - 43)^+$ ions.

TABLE 3. Mass Numbers (m/z) of the Parental Ions Calculated from the MD Spectra of the Daughter Ions of Compounds (I-VIII)

Daughter ion	Parental ions	Daughter ion	Parental ions
	I		IV
344	391, 376, 361	350	365
342	391, 374, 360	346	393, 376, 363
336	391	344	393, 376, 362
332	391, 376, 363	337	393
330	391, 376, 360, 348	335	393
328	391, 376, 360, 346	332	378, 362
326	391, 376, 358, 346	330	378, 362, 348
324	358, 342	328	393, 378, 360, 346
320	391	322	393, 337
316	391	314	376, 344
304	391, 358, 333, 319	304	393, 362, 337, 322
302	391, 360, 346, 332, 320	276	393, 337, 319
272	391, 360, 304, 302, 287	275	393, 378, 337, 293
232	391, 305, 302		V
208	391, 361, 236	366	381
190	391, 376, 360, 208	362	392, 379
	II	340	392, 378
364	407, 379	353	409
360	407, 392, 377	351	409
358	407, 390, 376	348	394, 378
346	407, 376	344	409, 394, 376, 362
344	392, 376, 362	338	409, 353
342	392, 374, 360	292	409, 351, 310
332	407, 392, 376, 362	291	409, 353, 309
330	407, 392, 376, 360		VI
328	407, 392, 376, 360	363	409, 392, 380
317	407	362	392, 379
304	407, 392, 376, 330, 322	360	392, 378
274	407, 328, 305	353	409
248	407, 392, 318	348	409, 394, 378
244	407, 274	346	394, 378, 364
232	392, 376, 362, 248	344	394, 376, 362
222	407, 392, 376, 252	342	409, 378, 353, 338
206	376, 360, 235	320	409, 378, 353, 338
	III	310	353
364	407, 379	304	409, 392, 353, 336, 322
360	407, 392, 377	291	409, 353, 320, 309
358	407, 390, 376		VII
352	407	320	348, 335
348	407, 392, 376		VIII
346	407, 392, 376, 364	353	396, 368
344	407, 392, 376, 362	350	396, 378, 368
342	407, 392, 374, 360	306	396
336	407, 376, 351	232	396, 376
321	407, 336	213	396, 378, 365, 241
283	407, 318	195	396, 378, 365, 213

The spectrum of the d_5-analog of monticamine (VIII) shows the occurrence of more than two processes for the appearance of these ions: in addition to the peaks of the $(M - CO{-}CD_3)^+$ ions there are the peaks of $(M - CO{-}CH_3)^+$ ions with a height ratio of 1:2. The MD spectra of both daughter ions – $(M - 43)^+$ and $(M - 46)^+$ – show, in addition to the above-mentioned sequence of elimination of particles – the peaks of the synchronous elimination of $COCH_3$ ($COCD_3$), while in the spectrum of the $(M - 46)^+$ ions there is a peak corresponding to the opposite sequence – $(M - CD_3{-}CO)^+$. These facts indicate that one of the pathways for the stabilization of $(M - CO)^+$ is simple cleavage in the N–Et group [$(M - 43)_1^+$ ions]. Another pathway includes the cleavage of the bonds of the bonds in rings B, C, and D and the splitting out of $\dot{C}H_3$ from the methoxy group at C-14 or C-16 (see Scheme 1). In agreement with this hypothesis, the energy of the metastable transition $(M - 28)^+ \rightarrow (M - 46)^+$ amounts to 2.55 eV and that of the $(M - 28)^+ \rightarrow (M - 43)^+$ transition to 6.31 eV. The $(M - 28)^+ \rightarrow (M - 43)^+$ transition in the spectrum of N-normonticamine (VII) shows a similar value (6.09 eV). The $(M - 28)^+$ and $(M - 43)^+$ ions are uncharacteristic for the dihydro derivatives (IV-VI) and the Δ^2-compounds.

An interesting feature of the spectra of monticamine and excelsine is the appearance of nitrogen-free fragments with m/z 305 (I) and 321 (III). In the spectrum of monticoline

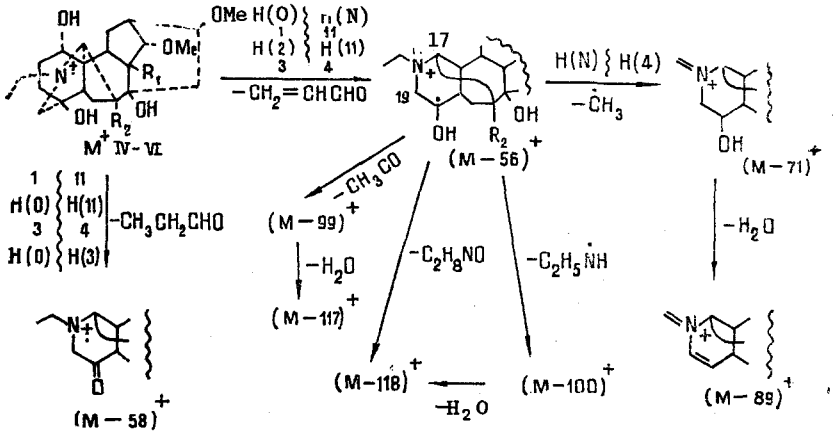
(II) the peak of the corresponding ion is weaker. In the spectrum of the d_5-analog (VIII) the m/z 305 peak has shifted by 1 m.u. In view of the single-stage nature of the $M^+ \rightarrow 306^+$ transition (according to the MD spectrum), this process is shown in the scheme for M^+ (VIII) (the intermediate stages of the isomerization of M^+ have been omitted). Then the ion with m/z 306 is converted into an ion with m/z 232. The spectra of (II) and (III) contain analogs of this with m/z 248.

It was mentioned above that the reason for the unusual distribution of the contributions of the main fragments in the spectra of the Δ^2-compounds (IX)-(XI) was the C-4–C-19 cleavage. Within the framework of this idea, scheme 1 shows an alternative mechanism of the formation of the $(M - CH_3)^+$ ions related to that which was given for the epoxy bases. Together with this, the differences in the structures of the initial and intermediate ions of the 3,4-epoxy and Δ^2-bases lead to the above-mentioned difference in the values of T for the $M^+ \rightarrow (M - CH_3)^+$ transitions.

A very important feature of the spectra of the epoxy compounds (I-III) is the presence of ions with m/z 112 having the composition $C_6H_{10}NO$. They can be represented as the result of the cleavage of the C-4–C-5, N–C-17, and C-1–C-2 bonds. In the spectra of the isomers (IX) and (X) the peaks of these ions are weaker. The breakdown of the m/z 112 ions by the elimination of CO leads to m/z 84 ions. Each of the spectra has the peak of an ion with m/z 98 of variable intensity, one of the components of which has the composition C_5H_8NO and is formed on the cleavage of the C-4–C-5, N–C-17, and C-2–C-3 bonds.

In the central part of the spectrum of monticoline (II) there is a series of peaks of moderate intensity that are not characteristic of the spectra of other epoxy bases. Thus, according to its MD spectrum, an ion with m/z 244 and composition $C_{15}H_{16}O_3$ has the following precursors: M^+ and 274 a.m.u. It can arise from M^+ by the splitting out of the C_1–C_4–C_{19}–N–C_2H_5 chain and the additional splitting out of $3H + H_2O$. The formation of the m/z 244 ion from the m/z 274 ion is extremely problematical, since the latter is a doublet, $C_{16}H_{20}NO_3 + C_{17}H_{24}NO_2$. Another nitrogen-free ion with m/z 317 ($C_{19}H_{25}O_4$) is formed in one stage from M^+ (II) by the loss of a $C_3H_8NO_2$ fragment.

Let us then pass to the characterization of the minor directions of the fragmentation of the dihydro bases (IV)-(VI). The most considerable of them are connected in some way or another with the fragmentation of ring A. The loss of a molecule of acrolein that is characteristic for the 1α-hydroxy bases (the $(M - 56)^+$ ions [8]) is accompanied here, in contrast to the C_{19} lycoctonine alkaloids, by the elimination of CH_3 from N–Et and the subsequent splitting out of a water molecule (Scheme 2). This sequence of stages is clearly confirmed by the MD spectra of the corresponding daughter ions. Another distinguishing characteristic of the spectra of (IV-VI) is the presence of $(M - 58)^+$ ions formed by the elimination of a molecule of propionaldehyde.



Scheme 2. Minor pathways of the fragmentation of the dehydrobases (IV-VI).

In the central parts of the spectra of (IV-VI) there are the peaks of the ions $(M - 118)^+$ and $(M - 117)^+$ with m/z 275 and 276 (IV) and 291 and 292 (V and VI). The fragments of odd mass numbers do not contain a nitrogen atom, and those with even mass numbers, together with a nitrogen-free component, contain the component $C_{17}H_{26}NO_2$ (IV) or $C_{17}H_{26}NO_3$ (V and VI). According to the MD spectrum, the $(M - 118)^+$ ions are formed either directly from the $(M - 56)^+$ ions or by the successive loss of a C_2H_6N particle and a molecule of water. The nitrogen containing ions $(M - 117)^+$ are preceded by $(M - 99)^+$ ions which arise from the $(M - 56)^+$ ions by the elimination of the acetyl radical at the expense of the C_3–C_4 chain.

EXPERIMENTAL

For the conditions of the mass-spectrometric experimental work, see [7]. PMR spectra were taken in $CDCl_3$ on a Tesla BS-567 A/100 MHz spectrometer with HMDS as internal standard (the chemical shifts are given in the δ-scale).

N-Normonticamine (VII). A solution of 0.5 g of monticamine in acetone–water (4:1; 50 ml) was treated with 0.5 g of $KMnO_4$ in acetone–water (1:1; 120 ml), and the mixture was stirred at room temperature for 15 h. The excess of permanganate was decomposed with sodium sulfite, the precipitate was separated from the solution, and the acetone was distilled off on the water bath. The aqueous residue was extracted with ether (5 × 30 ml), with ether–chloroform (1:1, 2 × 40 ml), with chloroform (8 × 30 ml), and with butanol (4 × 40 ml). The chloroform extract, after the solvent had been distilled off and the residue had been treated with chloroform, yielded a crystalline product (0.065 g) which was chromatographed on a column of deactivated alumina (1:100) with elution by benzene–methanol (0.5%).

Fractions 5-8 yielded a product with mp 210-213°C, M^+ 363. PMR spectrum: two 3-H singlets at 3.30 and 3.36 (OMe); no N–Et signal.

N-C_2D_5-Monticamine (VIII). A solution of 24 mg of normonticamine in 4 ml of dry acetone was treated with 0.05 ml of C_2D_5I and 30 ml of freshly calcined potash. The mixture was boiled in the water bath under reflux for 14 h. After 10 h, another 0.05 ml of C_2D_5I was added. After some time, the potash was separated off, the solvent was evaporated off, the residue was dissolved in 2.5% aqueous sulfuric acid, and the solution was made alkaline with sodium carbonate and was extracted with ether (5 × 7 ml). The ethereal fraction after the elimination of the solvent by distillation gave the d_5-analog of monticamine (M^+ 396).

Reaction of Monticamine with Iodotrimethylsilane. A mixture of 0.3 g of monticamine, 0.09 g of NaI, and 0.09 g of $(CH_3)_3SiCl$ in 20 ml of dry acetonitrile was heated in current of nitrogen for 17 h. Then it was poured into ice water and the mixture was made alkaline with sodium carbonate and was extracted with chloroform (5 × 40 ml). The chloroform extract was washed with an aqueous solution of sodium thiosulfate and with water and, after filtration, it was dried over anhydrous sodium sulfate. The solvent was distilled off and the residue (0.29 g) was chromatographed on a column of deactivated alumina (1:100) with elution by benzene–methanol (1.25%). Fractions 10-14 yielded a reaction product (0.03 g), which, from the elementary composition of the molecular ion, $C_{22}H_{34}NO_5I$, and the nature of its fragmentation under EI, corresponded to 3-iododihydromonticamine, while fractions 19-24 yielded an amorphous substance (0.11 g) with M^+ 391. PMR spectrum: N–$CH_2\underline{CH_3}$ 1.01 ppm (3H, triplet, J = 7 Hz), two methoxy groups at 3.25 and 3.29 ppm (singlets of 3H each), and two olefinic protons in the 5.8-5.9 ppm region (multiplet).

Reaction of Monticoline with Iodotrimethylsilane. A mixture of 0.3 g of monticoline, 0.09 g of NaI, and 0.09 g of $(CH_3)_3SiCl$ in 25 ml of dry acetonitrile was heated in a current of nitrogen for 17 h. The working up of the reaction products was similar to that described above. Fractions 24-31 yielded a crystalline product (0.09 g) with mp 193-195°C, M^+ 407. PMR spectrum: N–$CH_2\underline{CH_3}$ - 1.03 ppm (3H, triplet, J = 7 Hz); two methoxy groups at 3.28 and 3.31 ppm (singlets of 3H each); and two olefinic protons at 5.8-5.9 ppm (multiplet).

N-C_2D_5-Δ^2-Dihydromonticamine (XI). A mixture of 7 mg of N-C_2D_5-monticamine, 3 mg of NaI, 2.5 mg of $(CH_3)_3SiCl$ and 3 ml of dry acetonitrile was heated in a current of nitrogen for 17 h. The reaction mixture was worked up in a manner similar to that for (IX). An amorphous substance with M^+ 396 was obtained.

SUMMARY

The EI fragmentation of eleven C_{18}-diterpene bases with oxygen functions at C-4 has been investigated. The relative contributions of the processes of forming the $(M - CH_3)^+$

ions in the 3,4-epoxy- and the Δ^2-dihydrobases have been determined. The causes of the redistribution of the intensities of the peaks of the main fragments have been discussed and, on this basis, a mechanism has been put forward for the formation of the $(M - 15)^+$ and $(M - 31)^+$ ions. The characteristic nature of the values of A and T in transitions to the above-mentioned daughter ions has been shown.

In the region of medium and low mass numbers of the spectra, fragments have been revealed and characterized which are not characteristic of other types of lycoctonine bases, including nitrogen-free fragments.

Minor directions of the fragmentation of 4-hydroxy-C_{18}-diterpene bases pass through a stage of the formation of a (M − 56) ion.

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