MASS SPECTRA OF TETRAHYDROQUINAZOLINE AND TETRAHYDROQUINAZOLIN-4-ONE DERIVATIVES

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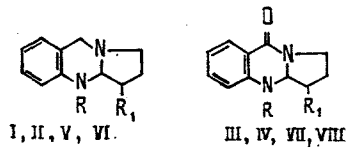
During a search for potential metabolites of the dihydroquinazoline alkaloids in the animal organism, we have studied the mass spectra of dihydro derivatives: those of deoxypeganine (I), of peganine (II), of deoxyvasicinone (III), and of vasicinone (IV) [1], and also their deuterium analogs (V-VIII).



I, II, V, VI

III, IV, VII, VIII

I, III. R, R_1 = H
V, VII. R = D; R_1 = H
II, IV. R = H; R_1 = OH
VI, VIII. R = D; R_1 = OD

The spectra of disubstituted 1,2,3,4-tetrahydroquinazolin-4-ones have been investigated by Bogentoft and Danielson [2], who established that the main direction of fragmentation of these compounds is due to the splitting out of the radical from C_2. Information on alicyclic derivatives of the systems considered is limited to the spectrum of a hexahydropyridoquinazoline [3]. The authors concerned [3] assumed that the 100% ion of this spectrum, $(M-57)^+$, arises as the result of the elimination of a polymethylene chain.

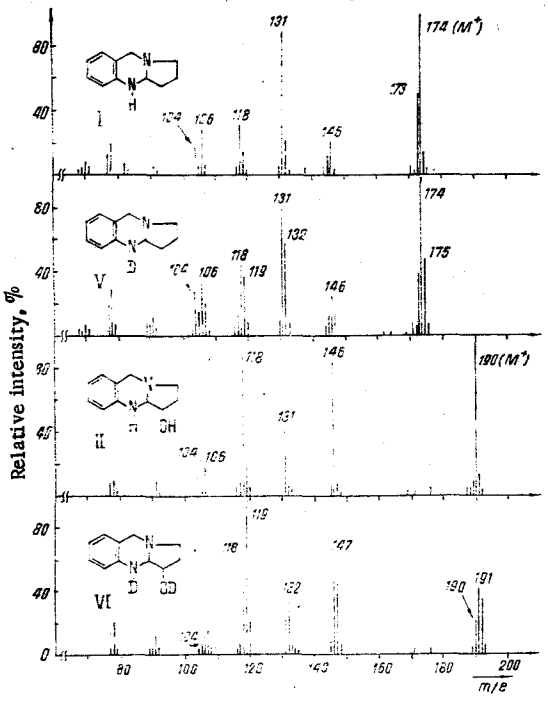


Fig. 1

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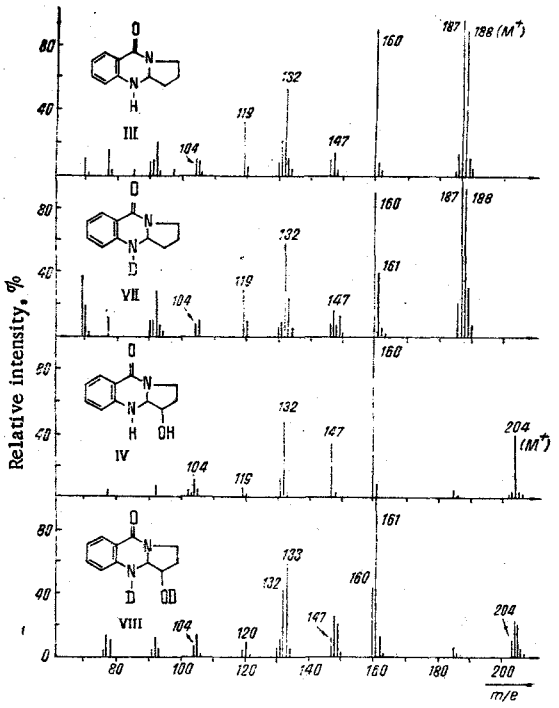
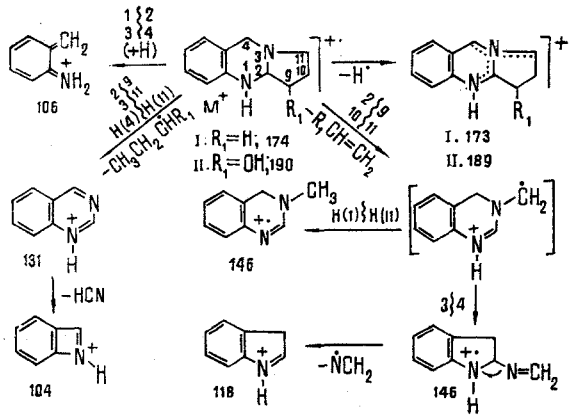


Fig. 2

The fragmentation of the tetrahydroquinazolines (I) and (II) and the tetrahydroquinazolinones (III) and (IV) shows a number of qualitative and quantitative differences. On comparing the hydroxy derivatives (II, IV) and the deoxy derivatives (I and III), qualitative differences between the spectra are mainly observed.

One of the most important quantitative differences in the spectra of (I) and (III) and of (II) and (IV) is the intensity of the peaks of the $(M-1)^+$ ion (Figs. 1 and 2). In spite of the fact that here there is an analogy with the behavior of deoxyvasicinone and vasicinone [4], in the cases under consideration a hydrogen atom is most probably split off not from C_9 but from C_2, which leads to the formation of the ions of protonated deoxyvasicinone and vasicinone (scheme). At the same time, the hypothesis of the influence of the OH group at C_9 on the intensity of the $(M-H)^+$ peak is not confirmed on passing to the spectrum of peganine [5, 6] – an alkaloid containing an OH group in this position. In its spectrum, the peak of the $(M-H)^+$ ion is the 100% peak, which is due to the stability of the quinazoline system arising as the result of the splitting out of hydrogen at C_4.



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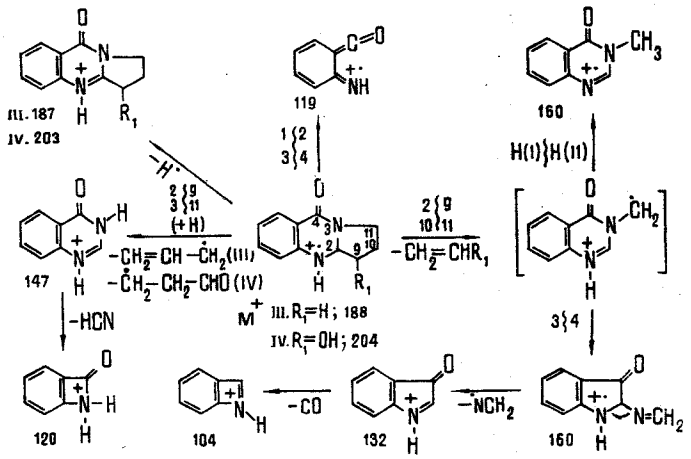

The absence of a π bond between N_1 and C_2 in the tetrahydro derivatives (I-VIII) stimulates the cleavage of the C_2-C_9 bond, the tendency to which increases when a hydroxy group is present at C_9. This cleavage then leads to the breakdown of ring C by the elimination of the C_9-C_{10} or the C_9-C_{11} chain. In all cases apart from that of dihydrodeoxypeganine (I), the first process leads to one of the most widely distributed fragments. The stability of the corresponding ion radical is possibly due to the fact that it rearranges in the form of 3-methyldihydroquinazoline or 3-methyldihydroquinazolin-4-one.

Below we give the elementary compositions of the main ions in the mass spectra of dihydropeganine (II), dihydrodeoxyvasicinone (III), and dihydrovasicinone (IV):

Calculated	Found	Composition
	Dihydropeganine	
146,0844	146,0845	$C_9H_{10}N_2$
131,0609	131,0585	$C_8H_7N_2$
118,0657	118,0675	C_8H_8N
106,0657	106,0670	C_7H_8N
	Dihydrodeoxyvasicinone	
188,0949	188,0930	$C_{11}H_{12}N_2O$
160,0637	160,0627	$C_9H_8N_2O$
147,0559	147,0556	$C_8H_7N_2O$
132,0449	132,0464	C_8H_6NO
131,0609	131,0615	$C_8H_7N_2$
120,0449	120,0429	C_7H_6NO
119,0371	119,0367	C_7H_5NO
104,0500	104,0487	C_7H_6N
92,0500	92,0489	C_6H_6N (~ 20%)
92,0261	92,0257	C_6H_4O (~ 80%)
	Dihydrovasicinone	
160,0637	160,0621	$C_9H_8N_2O$
147,0559	147,0560	$C_8H_7N_2O$
132,0449	132,0452	C_8H_6NO
119,0371	119,0344	C_7H_5NO
104,0500	104,0514	C_7H_6N

The elementary compositions of the ions, and also the shift of the peaks by one mass unit in the spectra of the deuterium analogs confirms that these fragments were formed by the elimination of a $CH_2=CHR_1$ molecule.

Some of the $(M - CH_2=CHR_1)^+$ ions decompose by the elimination of a fragment with 28 amu, which is confirmed by metastable peaks. The results of accurate measurements of the masses of the ions with m/e 118 (II) and 132 (III, IV) show that the composition of this fragment is CH_2N. Although the mechanism of its ejection may actually be simple (see scheme), the idea of a fragment in the form of a methyleneimine radical is unconvincing from the energy point of view and is compensated only by the stability of the even-numbered-electron fragment formed in this stage.

Thus, in the spectra of (III) and (IV) no elimination of C=O from the ion with m/e 160 takes place, in spite of the hypothesis of Luckner et al. [7] made in relation to the ion of 3-methylquinazolin-4-one. At the same time, in these spectra an ion of medium intensity with m/e 131 and with the composition C_8H_7N is observed. In all probability, it is formed as the result of the elimination of a formyl radical from the ion with m/e 160 (see scheme).

The elimination of CO is observed in the decomposition of some of the ions with m/e 132, which leads to a fragment with m/e 104 (C_7H_6N). Corresponding to the ion with m/e 132, ions with m/e 118 (I, and II), by losing HCN, are converted into fragments with m/e 91, as has been recorded with the aid of metastable peaks.

The splitting out of the C_9-C_{11} chain from M^+ is more characteristic in the quantitative respect for the tetrahydroquinazolines (I) and (II), particularly for (I). The qualitative differences between the tetrahydroquinazoline derivatives (I, II) and the tetrahydroquinazolin-4-one derivatives (III, IV) consist in the opposite direction of migration of the hydrogen atom in a decomposition process of the given type. This forms ions of protonated quinazoline with m/e 131 (I, II) or of protonated dihydroquinazolin-4-one with m/e 147 (III, IV) (see Scheme).

The ratios between the intensities of the polyisotopic peaks M^+ and m/e 147 in the spectrum of the deuterium analog of (VIII) approximately coincide (see Fig. 2). This indicates the predominant migration of the hydrogen of the hydroxy group to the charged fragment with 147 amu in the case of dihydrovasicinone (IV). In the formation of the analogous ion of dihydrodeoxyvasicinone (III), migration of hydrogen takes place from C_{10}.

All the spectra lack clear signs of further decomposition of the ions with m/e 131 and 147, although the relatively weak peaks of the ions with m/e 104 and 120 may show a possibility of the loss of a HCN molecule by the fragments.

The ion with the composition C_7H_5NO, m/e 119 (III, IV), can hardly be formed from the ion with m/e 147 by the elimination of H_2CN, since the successive elimination of two radicals from M^+ is energetically unfavorable. This ion most probably arises from M^+ as a result of decomposition of the retrodiene type, as has been established in the case of the spectra of 1H-dihydroquinazolin-4-ones [8] and also of tetrahydroquinazolin-4-ones [2]. In the case of compounds (I) and (II), the retrodiene decomposition takes place with the migration of a hydrogen atom to the charged fragment. Judging from the shift of the ion with m/e 106 by two mass units in [D]dihydropeganine (VI), the source of the migrating particle is mainly the hydroxy group.

The ion with m/e 92 in the spectrum of (III) is a doublet. A fragment with the composition C_6H_6N ($\approx 20\%$) is formed from the ion with m/e 120 by the elimination of CO, and a fragment with the composition C_6H_4O ($\approx 80\%$) from the ion with m/e 119 by the ejection of HCN.

Experimental conditions: MKh 1303 mass spectrometer (direct introduction of the sample), temperature of the inlet system 100-120°C, ionizing voltage 40 V, emission current 50 μA. Deuteration was carried out by short immersion of the samples in CD_3OD solution. The accurate masses were measured on a Varian MAT 311 instrument (Chemical Faculty of Tashkent State University) and a MS 902 instrument (Institute of Bioorganic Chemistry of the Academy of Sciences of the USSR).

SUMMARY

The main directions of fragmentation of 2,3-trimethylenetetrahydroquinazolines (I, II) and 2,3-trimethylenetetrahydroquinazolin-4-ones (III, IV) are the elimination of the C_9-C_{10} chain with the subsequent splitting out of a methyleneimine radical and the elimination of the C_9-C_{11} chain with the migration of hydrogen to the neutral (I, II) or the charged (III, IV) fragment.

LITERATURE CITED

1. B. Kh. Zharekeev, M. V. Telezhenetskaya, Kh. N. Khashimov, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 679 (1974).
2. C. Bogentoft and B. Danielson, J. Heterocyclic Chem., 9, 193 (1972).
3. J. S. Fitzgerald, S. R. Johns, J. A. Lamberton, and A. H. Redcliffe, Aust. J. Chem., 19, 151 (1966).
4. V. N. Plugar', T. T. Gorovits, N. Tulyaganov, and Ya. V. Tashkes, Khim. Prirodn. Soedin., 250 (1977).
5. A. K. Bhatnagar and S. P. Popli, Ind. J. Chem., 4, 291 (1966).
6. A. P. Orekhov, The Chemistry of the Alkaloids [in Russian], Moscow (1955), p. 651.
7. M. Luckner, K. Winter, L. Nover, and J. Reish, Tetrahedron, 25, 2575 (1969).
8. S. C. Parkaschi, J. Bhattacharyya, L. E. Johnson, and H. Budzikiewicz, Tetrahedron, 19, 1011 (1963).