MASS SPECTRA OF 2,3-POLYMETHYLENE-3,4-DIHYDROQUINAZOLIN-4-ONES WITH SUBSTITUENTS AT C_9

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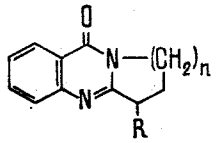
We have previously [1, 2] studied the mass spectra of tetrahydro derivatives of quinazolone alkaloids and have shown that the absence of a π-bond between N_1 and C_2 stimulates the cleavage of the C_2–C_9 bond.

We have now studied the mass spectra of derivatives of 2,3-trimethylene-3,4-dihydroquinazolin-4-one (I), 2,3-tetramethylene-3,4-dihydroquinazolin-4-one (IV), and 2,3-pentamethylene-3,4-dihydroquinazolin-4-one (III) with various substituents at C_9 in order to elucidate the influence of their nature on the fragmentation of ring C.



	a	b	c	d	e
I. $n = 1$,	R = H,	OH,	Br,	Cl,	OAc.
II. $n = 2$,	R = H,	OH,	Br,		OAc.
III. $n = 3$,	R = H,	OH,	Br,	Cl,	OAc.

The main directions of the decomposition of deoxyvasicinone (Ia) and vasicinone (Ib) have been considered previously [3].

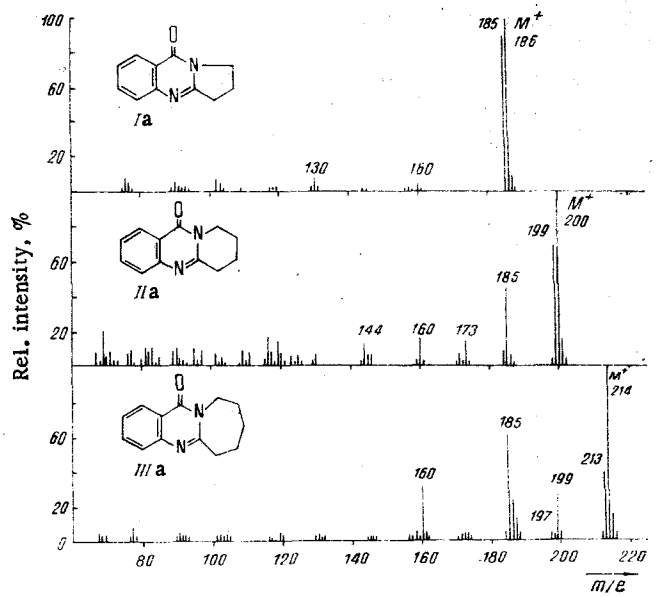


Fig. 1. Mass spectra of compounds of (Ia)-(IIIa).

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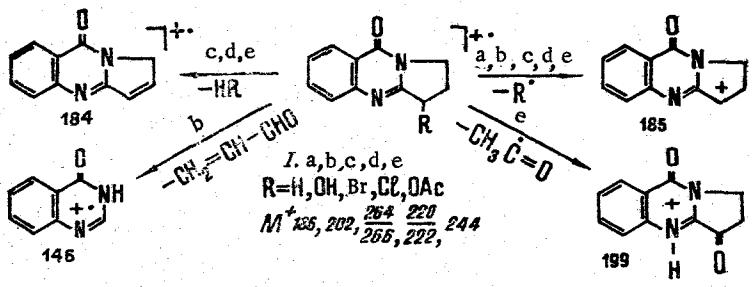
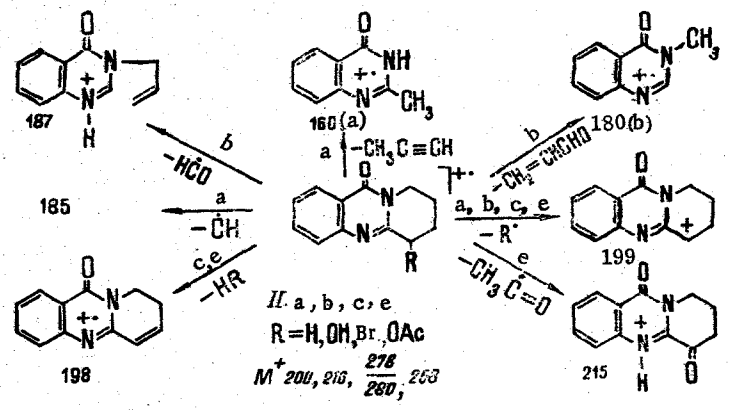
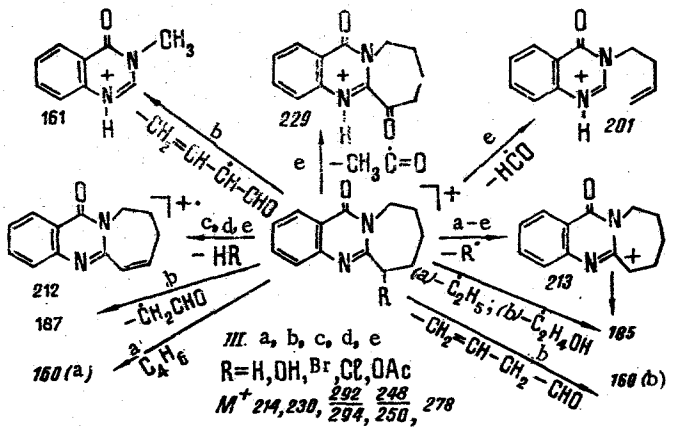
In the fragmentation of unsubstituted 2,3-polymethylene-3,4-dihydroquinazolin-4-ones a number of qualitative and quantitative differences are observed. One of the most important quantitative differences between the spectra of (Ia), (IIa), and (IIIa) is the intensity of the $(M - H)^+$ peak. Figure 1 shows a regular fall in this magnitude with expansion of the aliphatic ring and a simultaneous increase in the intensities of the peaks of the fragmentary ions in the same sequence. While in compound (Ia) the $(M - H)^+$ peak is comparable with the molecular peak (90 and 100%, respectively) and the intensities of the other fragmentary ions formed in the decomposition of the polymethylene chain (Fig. 1, Scheme 1) are extremely low, in compound (IIa) the peak corresponding to the ejection of a methyl radical (m/e 185) amounts to more than 40% of the molecular ion (Scheme 2). In compound (IIIa), in addition to a further fall in the intensity of the $(M - H)^+$ peak there is a considerable intensification of the fragments with m/e 199, 185, and 160 (a), which corresponds to the ejection of a unit containing one, two, and four of the carbon atoms of the alicyclic ring (Scheme 3).



Scheme 1



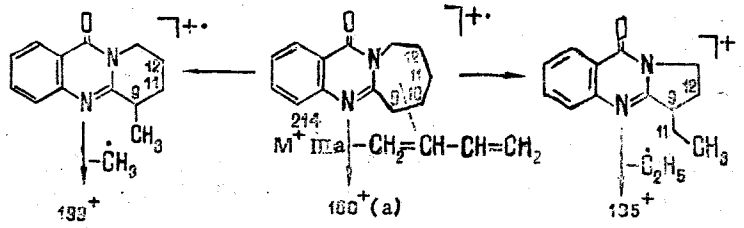
Scheme 2



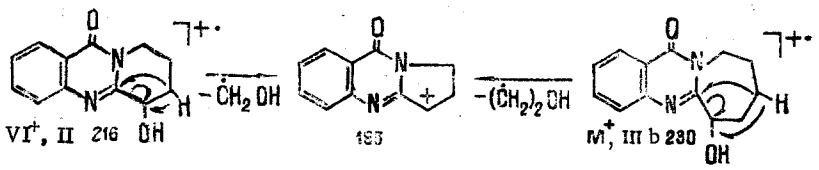
Scheme 3

Obviously, with an increase in the size of the alicyclic ring the possibility of ring reclosure is realized which, in the case of compound (IIIa) can be illustrated by Scheme 4. As can be seen from the Scheme, the initial act for the contraction of the ring is the cleavage of the C_9—C_{10} bond. The ejection of a methyl radical from M^+ of compound (IIa) takes place by a similar route.

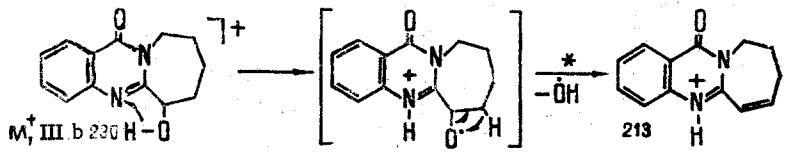
The cleavage of the corresponding bond in a compound with a five-membered ring (Ia) cannot be accompanied by the formation of a stable fragment with the elimination of a hydrocarbon chain, which explains the increased intensity of the $(M - H)^+$ peak in this case.



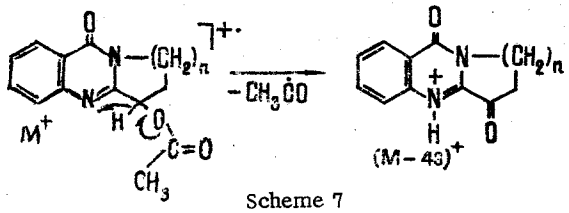
Scheme 4



Scheme 5



Scheme 6



Scheme 7

The mass spectra of the hydroxy derivatives (Ib-IIIb) reveal some differences in the direction of decomposition as compared with the unsubstituted compounds (Fig. 2). By analogy with the 2,3-polymethylene-1,2,3,4-tetrahydroquinazolines [2], the presence of an OH group at C_9 increases the tendency of the molecular ions of compounds (Ib-IIIb) to undergo C_2—C_9 cleavage. In vasicinone (Ib) this act is accompanied by the elimination of the whole polymethylene chain with the formation of the 3,4-dihydroquinazoline-4-one cation with m/e 146 [3]. As compared with vasicinone, the fragmentation pathways of the hydroxy compounds with six- and seven-membered rings C, including the elimination of the C_9—O element, are more diverse. The strongest fragmentary ions in the spectra of (IIb) and (IIIb) arise as the result of the elimination of a formyl radical (Schemes 2 and 3). A measurement of the elementary composition of the $(M - 29)^+$ ions showed that in the case of compound (IIb) this fragment was formed completely by the elimination of a HCO particle, while in the case of compound (IIIb) a doublet appeared which included ~5% of $(M - C_2H_5)^+$ ions (Table 1).

Both compounds are characterized by stable 3-methyl-3,4-dihydroquinazolin-4-one fragments with m/e 160 (b), which are isomeric with the 160 (a) ions in the spectra of compound (IIa)

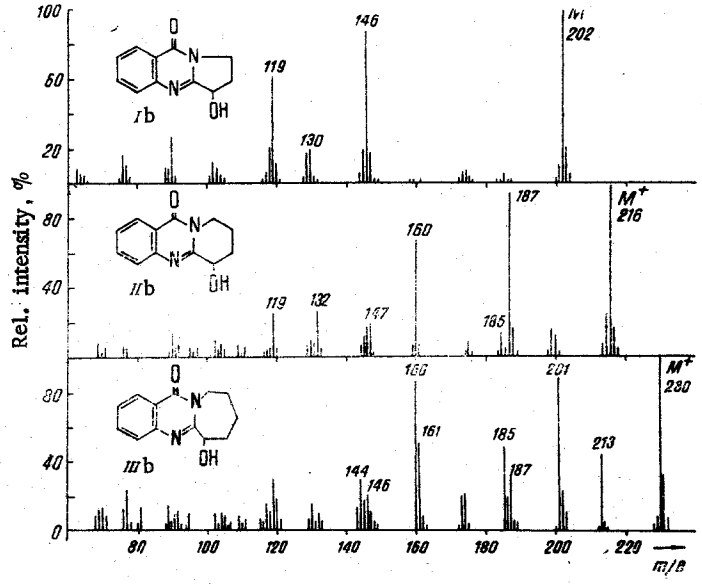


Fig. 2. Mass spectra of compounds (Ib)-(IIIb).

and (IIIa). The formation of these ions in the spectrum of vasicinone is unlikely because of the deficiency of hydrogen atoms in the fragment split off. In addition to ions with m/e 160, the spectrum of compound (IIIb) (Fig. 3) contains the protonated form with m/e 161 (Scheme 3).

The less common methods of losing the elements of ring C together with the substituent at C_9 include the elimination of hydroxymethylene radicals, which leads to a cyclic ion with m/e 185 having the same structure as in the case of the unsubstituted compounds (Ia-IIIa). The mechanism of this process is shown in Scheme 5.

It can be seen from Schemes 2 and 3 that a fundamental role in the stabilization of a series of fragments is played by the protonation of the N_1 atom. We have directed our attention to the unusually high intensity of the $(M - OH)^+$ peaks, particularly in the spectrum of (IIIb) (Fig. 2). This clearly shows the metastable transition $M^+ \rightarrow (M - OH)^+$, which is evidence in favor of the rearrangement nature of this process (Scheme 6).

TABLE 1. Elementary Compositions of the Ions

Found	Calculated	Composition	Origin
		IIb	
216,0913	216,0899	$C_{12}H_{12}N_2O_2$	M^+
187,0895	187,0872	$C_{11}H_{11}N_2O$	$(M-CHO)^+$
185,0701	185,0714	$C_{11}H_9N_2O$	$(M-CH_2OH)^+$
160,0616	160,0636	$C_9H_8N_2O$	$(M-CH_2=CH-CHO)^+$
		IIIb	
230,1059	230,1060	$C_{13}H_{14}N_2O_2$	M^+
213,1027	213,1028	$C_{13}H_{13}N_2O$	$(M-OH)^+$
I 201,1041	201,1030	$C_{12}H_{13}N_2O$	$(M-CHO)^+$ 95%
II 201,0679	201,0663	$C_{11}H_9N_2O_2$	$(M-C_2H_5)^+$ 5%
I 187,0878	187,0871	$C_{11}H_{11}N_2O$	$(M-CH_2CHO)^+$ 95%
II 187,0532	187,0507	$C_{10}H_7N_2O_2$	$(M-C_3H_7)^+$ 5%
I 185,0694	185,0715	$C_{11}H_9N_2O$	$(M-C_2H_4OH)^+$ 95%
II 185,1054	185,1078	$C_{12}H_{13}N_2$	$(M-HCO-CO)^+$ 5%
161,0674	161,0715	$C_9H_9N_2O$	$(M-C_4H_5O)^+$
160,0618	160,0637	$C_9H_8N_2O$	$(M-C_4H_6O)^+$
		IIIe	
272,1139	272,1160	$C_{15}H_{16}O_3N_2$	M^+
229,0976	229,0977	$C_{13}H_{13}O_2N_2$	$(M-CH_2CHO)^+$
212,0907	212,0949	$C_{13}H_{12}ON_2$	$(M-C_2H_4O_2)^+$

In the spectra of the compounds in which R = Hal or $OCOCH_3$, the processes of breakdown of ring C are suppressed (Fig. 3), which is connected with the volume of the substituent and the stability of the charged fragments formed. In the spectra of the halogen-constituted compounds (Ic-IIIc) and (Id) and (IIId), the maximum ions are the $(M - X)^+$ ions, and the contribution of the process of the splitting off HX is relatively small. Below we give the relative intensities of the main peaks in the spectra of the halogen-containing compounds (%):

Compound	M^+	$(M-X)^+$	$(M-HX)^+$
R=Br			
I c	20/20	100	14
II c	24/24	100	30
III c	16/16	100	20
R=Cl			
I d	37/95	100	25
III d	29/88	100	12

This fact shows that the fragmentation of the compounds under consideration is similar to the behavior of benzyl halides [4] and differs from the decomposition of cycloalkyl halides, in the spectra of which the splitting off of HCl from M^+ considerably exceeds the splitting off of the chlorine atom [5].

In the spectra of the acetyl derivatives (Ie-IIIe), the main peaks are the peaks of the ions $(M - 43)^+$ (Fig. 3). The compositions of these fragments were confirmed by measuring the accurate masses of the ions (Table 1). We also explain the preferential formation of this fragment by the possibility of the protonation of the nitrogen atom according to Scheme 7.

The presence of conjugation explains the high stability of the proposed structure. The contributions of the processes in which acetic acid and an acyl radical are split off $(M-60)^+$ and $(M - 69)^+$, respectively, depend on the size of the alicyclic ring (Fig. 3). The corresponding peaks reach their maximum intensity in the case of compound (IIIe) (I_{212} = 56%). This is probably connected with the greater mobility of the seven-membered ring.

EXPERIMENTAL

MKh-1303 mass spectrometer (direct introduction of the sample), temperature of inlet system 100-120°C, ionizing voltage 40 V, emission current 50 μA. The accurate masses of the ions were measured on a MKh-1310 instrument using a system for the direct introduction of the sample at an ionizing voltage of 70 V, a collector current of 80 μA, and a temperature of the ionizing chamber of 70°C.

Compound (I-IIIa) and (IIId) were synthesized as described previously [6], and (Id) by the method of Morris et al. [7]. The synthesis of α-bromo-2,3-trimethylene-3,4-dihydroquina-

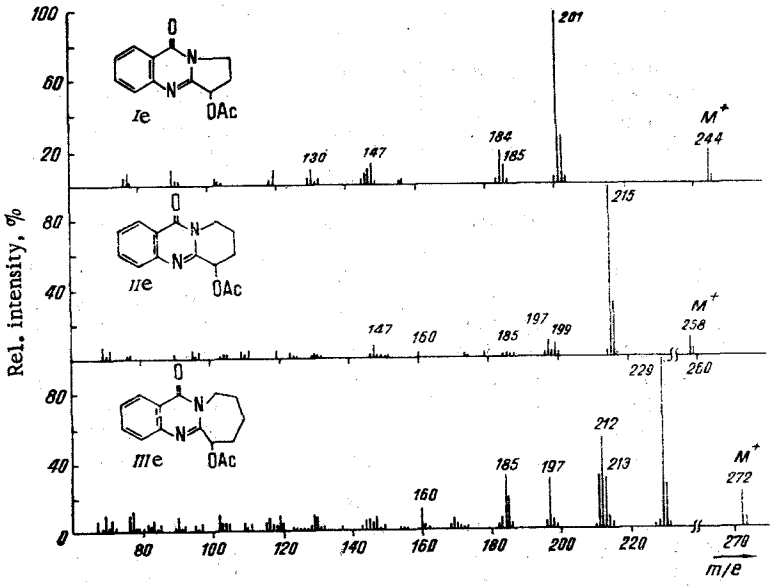


Fig. 3. Mass spectra of compounds (Ie)-(IIIe).

zolin-4-one (Ic) and the corresponding tetramethylene and pentamethylene compounds (IIc, IIIc) was carried out by the method of Dewi et al. [8].

α-Hydroxy-2,3-tetramethylene-3,4-dihydroquinazolin-4-one (IIv). A mixture of 30 mg of freshly-fused sodium acetate and 0.2 ml of glacial acetic acid was heated until the sodium acetate had dissolved completely. Then 50 mg of α-bromo-2,3-pentamethylene-3,4-dihydroquinazolin-4-one (IIc) was added to the reaction mixture and it was heated at 120-130°C for 10 h. Then it was cooled, decomposed with water, and extracted with chloroform. After the solvent had been distilled off, the residue was chromatographed on a column of alumina (with chloroform as eluent). α-Acetoxy-2,3-tetramethylene-3,4-dihydroquinazolin-4-one (IIe) was isolated in the form of an oil. The saponification of this acetate with 5% caustic soda solution at 40-50°C yielded 15 mg [39% calculated on the (IIc)] of α-hydroxy-2,3-tetramethylene-3,4-dihydroquinazolin-4-one (IIb, amorphous substance).

Compounds (IIIe) (oil) and (IIIb) (amorphous substance) were obtained similarly.

SUMMARY

The main fragments in the mass spectra of the 2,3-polymethylene-3,4-dihydroquinazolin-4-one with six- and seven-membered alicyclic rings are formed by the decomposition of ring C through the stage of the cleavage of the C_9—C_{10} bond, while the compound with a five-membered ring ejects a hydrogen atom.

A hydroxy group at C_9 initiates the appearance of fragments due to the initial cleavage of the C_2—C_9 bond. In the spectra of the halogen and acetoxy derivatives the fragmentation of the alicyclic ring is suppressed and the main fragmentation pathway is the splitting out of the substituent. The hypothesis of the protonation of the N_1 nitrogen atom has been adopted to explain the stability of a number of the ions.

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