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MASS-SPECTROMETRIC STUDY OF 3,9-DIAZABICYCLO- AND 3,9-OXAAZABICYLO[3.3.1]NONANES*

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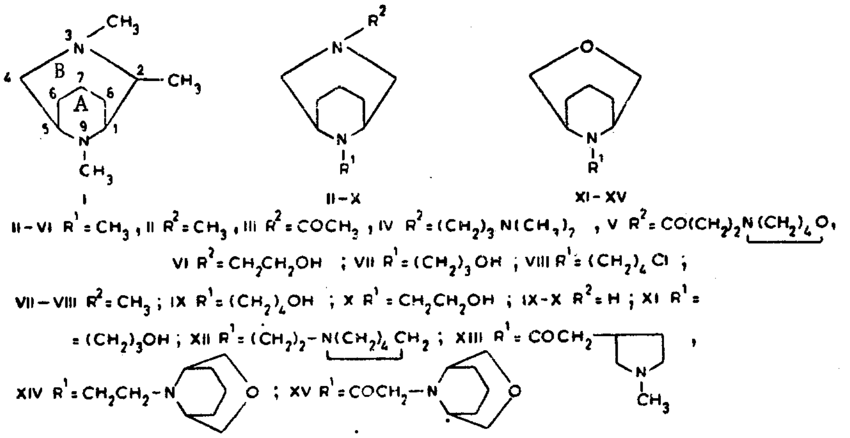
UDC 547.834.3'867:543.51

The mass spectra of substituted 3,9-diazabicyclo- and 3,9-oxaazabicyclo[3.3.1]-nonanes were studied as a function of competitive distribution of the charge between the N_3 and N_9 and O_3 and N_9 atoms and the properties of the substituents attached to the heteroatoms. It is shown that a characteristic peculiarity of the fragmentation of 3,9-diazabicyclo[3.3.1]nonanes is fragmentation of the molecular ion with an open structure that is formed by cleavage of the C_1—C_2 bond. The formation of an amine fragment with retention of the bicyclic structure with an exocyclic double bond attached to the quaternary N_9 atom is characteristic for 3,9-oxaazabicyclo[3.3.1]nonanes. It is shown that this sort of behavior of the investigated compounds is determined by their structures and the properties of the heteroatoms in the saturated bicyclic systems.

In a continuation of our research on the mass-spectrometric fragmentation of saturated bicyclic amines [2] we have studied the mass spectra of 3,9-diazabicyclo[3.3.1] nonanes I-X and 3,9-oxaazabicyclo[3.3.1]nonanes XI-XV.



I

II–X

XI–XV

II–VI $R^1 = CH_3$, II $R^2 = CH_3$, III $R^2 = COCH_3$, IV $R^2 = (CH_2)_3N(CH_3)_2$, V $R^2 = CO(CH_2)_2N(CH_2)_4O$, VI $R^2 = CH_2CH_2OH$; VII $R^1 = (CH_2)_3OH$; VIII $R^1 = (CH_2)_4Cl$; VII–VIII $R^2 = CH_3$; IX $R^1 = (CH_2)_4OH$; X $R^1 = CH_2CH_2OH$; IX–X $R^2 = H$; XI $R^1 = (CH_2)_3OH$; XII $R^1 = (CH_2)_2-N(CH_2)_4CH_2$; XIII $R^1 = COCH_2-$, XIV $R^1 = CH_2CH_2-N$; XV $R^1 = COCH_2-N$

According to the results of chemical investigations [3] and data from the PMR spectra [4], the piperazine ring in I-X exists primarily in the chair conformation. We expected that both heteroatoms in derivatives I-X and their oxygen analogs XI-XV would have a specific effect on the character of the fragmentation of the bicyclic system as a function of the competitive distribution of the charge between them and on the properties of the substituents attached to these atoms. The present research was therefore undertaken to study the fragmentation of I-XV under electron impact.

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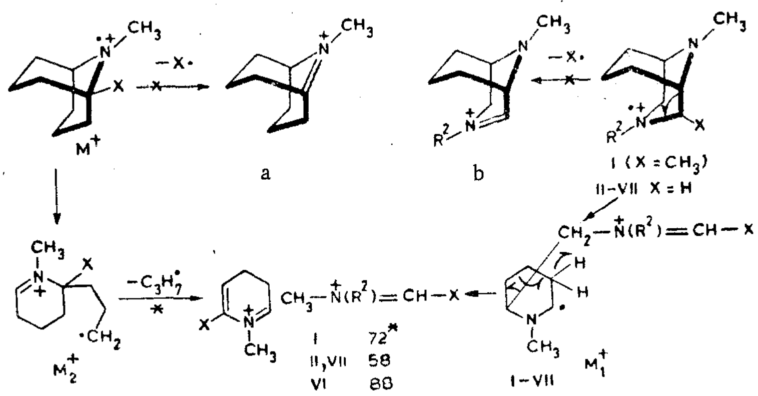
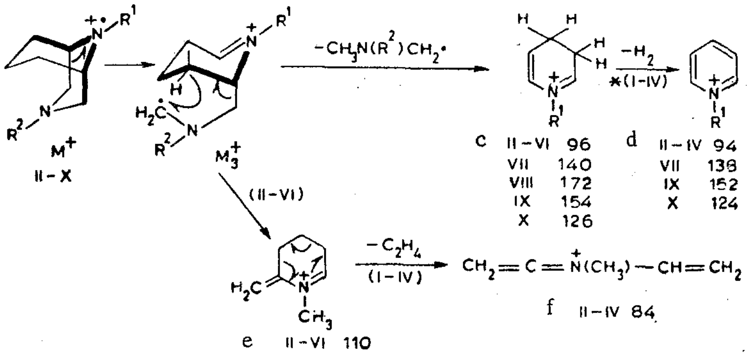
We found that the fragmentation of I-XV has a great deal in common with the fragmentation of derivatives of 9-methyl-9-azabicyclo[3.3.1]nonanes and 9-oxabicyclo[3.3.1]nonanes, which were investigated in [5, 6]. We also found a similarity in the fragmentation of derivatives I-XV and some analogs in series of 1,2,6-substituted piperazines and piperidines [7-9]. In addition, there are specific principles that are characteristic only for this class of compounds in the behavior under electron impact of piperidinopiperazines I-X and piperidinomorpholines XI-XV.

An important sterospecific peculiarity in the fragmentation of the analogous nitrogen-containing bicyclic compounds that was not discussed in [5] follows from an analysis of the mass spectra of I-X and analogs of the 9-methyl-9-azabicyclo[3.3.1]nonane series. The characteristic (for α-substituted nitrogen heterocycles) detachment of a substituent from the α position with the formation of amine fragments of the a and b type with an endocyclic double bond at the nitrogen atoms in the rings is not observed for these compounds (Scheme 1).

Scheme 1



Scheme 2



This behavior of I and its analogs [5] is most likely due to steric factors. In the case of the formation of $[M-X]^+$ or $[M-H_\alpha]^+$ ions, which suggests the presence of double bonds at the nitrogen atoms in the A or B rings, the bicyclic system evidently experiences such pronounced distortions of the interatomic bond angles at the nodal C_1 and C_5 atoms that it cannot exist. The fragmentation of I-X therefore takes place from the molecular ions with an M_1^+, M_2^+, or M_3^+ open structure.

The maximum peak in the mass spectra of I-X at energies of 70 and 12 eV corresponds to ion c, which is resistant to further fragmentation if substituents with a long alkyl chain are attached to the N_9 atom. The stability of I-X with respect to electron impact at an electron energy of 70 eV (see Table 1) depends substantially on the character of the substituents attached to both nitrogen atoms; this can be explained by the mutual effect of both heteroatoms on the fragmentation of the bicyclic system. From general principles it may be concluded that localization of the charge on the N_3 and N_9 atoms is equally probable in the ionization of the molecules of the investigated compounds. However, the primary

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*Here and subsequently, the numbers that characterize the fragments in the schemes and in the text are the mass-to-charge ratios.

TABLE 1. Mass Spectra of I-XV at Electron Energies of 70 (a) and 12 eV (b)

Compound	m/e values (relative intensities of ion peaks in % relative to maximum peak)
1	2
I a)	169 (6), 168 (35), 154 (3), 153 (7), 140 (8), 139 (8), 112 (6), 111 (7), 110 (10), 98 (15), 97 (18), 96 (100), 95 (8), 94 (6), 84 (5), 83 (5), 82 (10), 81 (2), 73(3),72 (48), 71 (2), 70 (8), 58 (8), 57 (24), 56 (8), 55 (7), 42 (22), 41 (8); $W_M=8{,}8\%$
I b)	169 (12), 168 (100), 154 (2), 112 (6), 111 (9), 110 (4), 98 (14), 97 (17), 96 (88), 95 (14), 74 (8), 73 (4), 72 (56), 58 (2), 57 (5), 56 (2); $W_M=29\%$
II a)	155 (4), 154 (41), 153 (4), 112 (3), 111 (6), 110 (12), 109 (2), 108 (4), 98 (4), 97 (16), 96 (100), 95 (8), 94 (6), 84 (5), 83 (4), 82 (100), 81 (2), 71 (2), 70 (6), 69 (1), 68 (5), 58 (16), 57 (20), 56 (4), 55 (6), 44(6), 43 (5), 42 (18), 41(8); $W_M=12{,}5\%$
II b)	155 (8), 154 (66), 97 (16), 96 (100), 59 (2), 58 (12); $W_M=32\%$
III a)	183 (4), 182 (12), 111 (4), 110 (8), 109 (8), 108 (8), 107 (7), 98 (5), 97 (12), 96 (100), 95 (4), 94 (6), 84 (2), 83 (5), 82 (6), 81 (3), 72 (8), 70 (5), 58 (3), 57 (10), 44 (4), 43 (6), 42 (10); $W_M=5\%$
III b)	183 (6), 182 (38), 109 (14), 97 (8), 96 (100), 72 (6); $W_M=22\%$
IV a)	226 (3), 225 (38), 195 (6), 181 (2), 180 (4), 168 (9), 167 (3), 154 (8), 153 (10), 140 (6), 139 (8), 129 (9), 128 (6), 117 (4), 116 (2), 115 (6), 111 (8), 110 (14), 109 (8), 108 (4), 98 (6), 97 (23), 96 (100), 95 (6), 94 (6), 86 (6), 85 (10), 84 (12), 83 (6), 82 (9), 81 (3), 72 (8), 71 (4), 70 (10), 59 (6), 58(100), 57 (14), 56 (6), 55 (8), 44 (8), 43 (9), 42 (21), 41 (12); $W_M=6{,}8\%$
IV b)	226 (16), 225 (90), 195 (7), 194 (41), 181 (6), 180 (16), 168 (7), 167 (5), 154 (42), 153 (14), 129 (48), 117 (24), 116 (4), 115 (28), 111 (22), 110 (42), 97 (36), 96 (85), 85 (14), 84 (10), 72 (8), 59 (14), 58 (100); $W_M=13{,}4\%$
V a)	282 (2), 281 (6), 263 (6), 251 (10), 238 (4), 196 (3), 195 (6), 194 (3), 142 (4), 141 (2),140 (5), 139 (7), 111 (4), 110 (12), 109 (16), 108 (6), 100 (33), 98 (34), 97 (20), 96 (100), 95 (2), 94 (6), 82 (6), 158 (9), 157 (10), 156 (10), 155 (8), 42 (16), 41 (6); $W_M=1{,}9\%$
V b)	282 (4), 281 (20), 264 (3), 263 (20), 252 (6), 251 (34), 250 (4), 238 (6), 196 (4), 195 (3), 194 (12), 110 (7), 109 (22), 98 (24), 97 (12), 96 (100); $W_M=7\%$
VI a)	185 (4), 184 (15), 183 (3), 167 (2), 166 (5), 154 (11), 153 (12), 141 (3), 139 (6), 112 (6),111 (7), 110 (2), 109 (3), 108 (9), 98 (4), 97 (23), 96 (100), 95 (12), 94 (14), 90 (6), 88 (36), 83 (6), 82 (16), 81 (6), 70 (12), 68 (7), 58 (4),57(54), 56 (10), 55 (10), 54 (4), 45 (4), 44 (10), 43 (4), 42 (36), 41 (12); $W_M=3\%$
VI b)	185 (4), 184 (28), 167 (2), 166 (10), 154 (12), 153 (12), 139 (4), 126 (4), 111 (4), 110 (6), 109 (4), 97 (14), 96 (100), 95 (14), 94 (4), 90 (10), 88 (36), 58 (2), 57 (5), 56 (2); $W_M=10\%$
VII a)	199 (5), 198 (25), 154 (2), 153 (4), 141 (12), 140 (100), 139 (2), 138 (3), 124 (4), 111 (2), 110 (6), 109 (2), 97 (8), 96 (12), 82 (3), 70 (4), 69 (4), 58 (6), 57 (5), 42 (7), 41 (7); $W_M=11\%$
VII b)	199 (7), 198 (36), 141 (12), 140 (100), 97 (7), 96 (7); $W_M=21\%$
VIII a)	232 (3), 231 (1), 230 (6), 175 (4), 174 (40), 173 (12), 172 (100), 171 (3), 153 (3), 152 (2), 138 (8), 110 (6), 98 (4), 97 (7), 96 (4), 84 (2), 83 (2), 82 (4), 70 (7), 69 (6), 68 (4), 67 (5), 58 (12), 55 (4), 42 (4), 41 (2); $W_M=3{,}5\%$
VIII b)	232 (6), 231 (3), 230 (18), 174 (31), 173 (12), 172 (100), 171 (4), 153 (4), 152 (2), 58 (3); $W_M=13\%$
IX a)	199 (3), 198 (16), 197 (2), 168 (2), 156 (23), 155 (14), 154 (100), 140 (4), 139 (8), 138 (5), 124 (6), 110 (12), 98 (7), 97 (12), 96 (17), 84 (8), 83 (9), 82 (22), 71 (4), 70 (6), 69 (8), 68 (7), 67 (3), 56 (10), 55 (12), 54 (6), 44 (6), 43 (4), 42 (10), 41 (14); $W_M=4{,}5\%$
IX b)	199 (4), 198 (24), 156 (4), 155 (12), 154 (100), 140 (8), 139 (6), 124 (4), 110 (3), 98 (4), 97 (5), 96 (12), 82 (4); $W_M=12{,}5\%$
X a)	171 (2), 170 (10), 154 (3), 153 (16), 140 (10), 139 (22), 128 (16), 127 (22), 126 (100), 125 (4), 124 (8), 111 (4), 110 (40), 109 (4), 108 (8), 98 (8), 97 (16), 96 (26), 95 (4), 94 (6), 84 (8), 83 (18), 82 (16), 81 (10), 70 (8), 69 (12), 68 (10), 67 (6), 57 (6), 56 (22), 55 (14), 54 (8), 53 (4), 45 (10), 44 (34), 43 (6), 42 (18), 41 (20); $W_M=1{,}8\%$
X b)	171 (3), 170 (14), 154 (4), 153 (34), 140 (8), 139 (16), 128 (22), 127 (20), 126 (100), 110 (8), 109 (3), 108 (4), 98 (3), 97 (7), 96 (9), 83 (17); $W_M=5{,}0\%$
XI a)	186 (10), 185 (42), 155 (7), 154 (7), 141 (24), 140 (100), 138 (4), 125 (2), 124 (22), 111 (11), 110 (42), 98 (7), 97 (22), 96 (12), 95 (3), 84 (4), 83 (8), 82 (12), 81 (4), 70 (8), 69 (12), 68 (7), 67 (4), 59 (4), 58 (4), 57 (18), 56 (13), 55 (12), 54 (6), 42 (12), 41 (18); $W_M=9\%$

TABLE 1 (continued)

1	2
XI b)	186 (18), 185 (48), 155 (26), 141 (48), 140 (100), 124 (10), 111 (6), 110 (14), 97 (14), 96 (7); $W_M = 16\%$
XII a)	239 (0,6), 238 (4), 154 (3), 141 (8), 140 (100), 112 (3), 111 (1), 110 (3), 99 (8), 98 (96), 83 (2), 70 (4), 69 (5), 68 (2), 67 (2), 56 (3), 55 (7), 54 (2); $W_M = 1{,}5\%$
XIII a)	253 (2), 252 (8), 170 (4), 169 (2), 139 (3), 138 (7), 98 (4), 97 (6), 96 (12), 85 (4), 84 (42), 83 (100), 82 (10), 70 (4), 69 (3), 68 (2), 58 (4), 57 (8), 56 (3), 55 (8), 44 (5), 43 (8), 42 (12), 41 (8); $W_M = 2{,}9\%$
XIII b)	253 (6), 252 (36), 170 (6), 169 (4), 97 (4), 96 (6), 84 (64), 83 (100); $W_M = 15\%$
XIV a)	280 (2), 279 (0,2), 141 (10), 140 (100), 110 (2), 109 (2), 108 (1), 86 (4), 85 (1), 84 (2), 56 (4), 55 (8), 43 (3), 42 (4), 41 (3); $W_M = 1{,}3\%$
IX b)	280 (10), 141 (12), 140 (100), 86 (4); $W_M = 7{,}9\%$
XV a)	295 (0,6), 294 (1,8), 249 (2), 141 (12), 140 (100), 111 (4), 110 (6), 97 (2), 96 (4), 86 (3), 71 (2), 70 (3), 69 (3), 57 (3), 56 (4), 55 (7), 54 (2), 43 (4), 42 (5), 41 (7); $W_M = 1\%$
XV b)	295 (0,5), 294 (4,5), 249 (2), 141 (12), 140 (100), 110 (2); $W_M = 3{,}7\%$

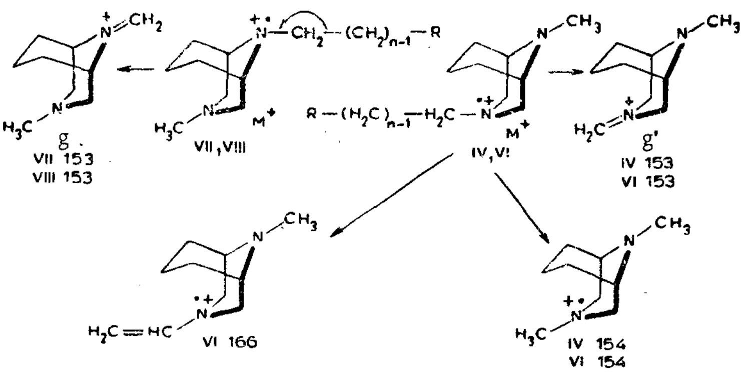
formation of ion c constitutes evidence that either the charge in the molecular ions is concentrated primarily on the N_9 atom or that migration of the charge to this atom, which is promoted by the para orientation of the heteroatoms relative to one another, is possible in the case of cleavage of the $C_1{-}C_2'$ or $C_1{-}C_5$ bond. In the case of fragmentation of 1,2,6-substituted piperidines [8] an ion of the c type is formed in high yield as a result of the process $M_2^+ \rightarrow c$ only in the spectrum at a high electron energy (70 eV) [5].

Data from a comparison of the intensities of the peaks of ion c and the $CH_2{=}\overset{+}{N}(CH_3)_2$ fragment (58) that is characteristic for tertiary amines indicate the ease with which the process $M_2^+ \rightarrow c$ occurs. In the fragmentation of IV, which has a propylamino group attached to the N_3 atom both of these fragments are formed directly from the molecular ion. It follows from the mass spectra of this derivative that the intensities of the peaks of ions with m/e 58 and 96 depend to the same extent on the ionizing electron energy, which was varied from 12 to 70 eV.

Peaks of fragments with m/e 70, 58, 43, and 42, which are characteristic for the fragmentation of 1,2,6-trimethylpiperidine [9], are observed in addition to peaks of ions c-f (Scheme 2) in the spectra of I-VI in the region of mass numbers below m/e 80. Their appearance is due to fragmentation of the A ring.

In contrast to the fragmentation of the corresponding piperidine and piperazine analogs, the formation of energetically favorable amine fragments with exocyclic double bonds is expressed extremely weakly in the fragmentation of derivatives IV-IX with a long alkyl chain attached to the N_3 and N_9 atoms. The peaks corresponding to fragment ions g and g' (Scheme 3) in the spectra at an electron energy of 70 eV have low intensities and are not observed in the low-voltage spectra. An analysis of Dreiding molecular models shows that steric factors that hinder the formation of a double bond at the N_3 and N_9 atoms play a smaller role here than in the case of the formation of a and b ions. One should probably assume that in the

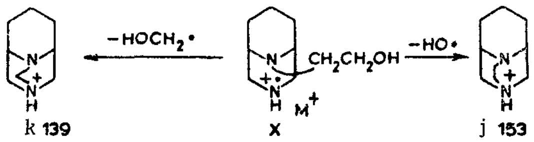
Scheme 3



fragmentation of IV and VI-VIII the $M^+ \rightarrow g\ (g')$ processes are suppressed by the energetically more favorable $M^+ \rightarrow c$ reaction. Only rearrangement fragmentation processes with the formation of ions with m/e 166 and 154 (Scheme 3) compete appreciably with this reaction.

In contrast to the fragmentation of analogs VII-IX, which have a longer alkyl chain, the appearance of $[M-OH]^+$ and $[M-CH_2OH]^+$ ions in the fragmentation of derivative X is due to the formation of tricyclic j and k structures with a common nodal atom, which correspond to protonated 3,5-(trimethylene)-1,4-diaza[2.2.2] octane and 3,5-(trimethylene)-1,4-diaza-[2.2.1]octane molecules (Scheme 4).

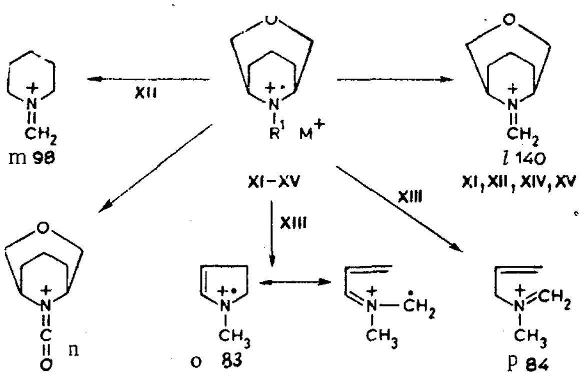
Scheme 4



The fact that a molecule of water is split out in the chemical transformations of derivative X to give 3,5-(trimethylene)-1,4-[2.2.2]octane constitutes evidence in favor of the formation of ions j (153) and k (139). Bulky substituents and groups with a long alkyl chain in the case of derivatives VII-IX, which have a methyl group attached to the N_3 atom or a multimember alkyl substituent attached to the N_9 atom, evidently hinder conversion of the B ring from the chair form to the boat conformation, from which the formation of structure j is only possible.

The behavior of 3,9-oxaazabicyclo[3.3.1]nonanes XI-XV under electron impact differs radically from the fragmentation of the diazabicyclo analogs. Cleavage of the C_1-C_2 bond in the molecular ion is not observed for these compounds, and the principal peak in the spectra of such compounds corresponds to fragment *l* with an exocyclic double bond at the N_9 atom (Scheme 5).

Scheme 5



The formation of ion *l* with a bicyclic structure is confirmed by a comparison of the relative intensities in the spectrum of XII of a peak of ion *l* (140) and a peak of cyclic piperidine amine fragment m (98). Both of these ions are formed by cleavage of the same C–C bond, and their intensities in the mass spectra depend on the change in the ionizing electron energy from 70 to 12 eV. The fragmentation of XI-XV with the primary formation of ion *l* with a bicyclic structure is evidently explained by the impossibility of charge migration from one ring heteroatom to the other in view of the considerable difference in the ionization potentials of the nitrogen and oxygen atoms in alicyclic compounds (~2.5 ev) [10].

It is interesting to note that amide fragment n is not formed in the fragmentation of XIII and XV even if the competitive formation of an ion of the *l* type does not occur. Hydrogen rearrangements with the formation of ions o and p (83 and 84), the peaks of which also retain their high intensities in the low-voltage spectrum, occur in the fragmentation of XIII.

One important peculiarity in the fragmentation of 3,9-oxaazabicyclo[3.3.1]nonanes follows from an analysis of the spectra of XI-XV. We observed that the intensity of the molecular-ion (M^+) peak in the spectra of XII and XIV, in the fragmentation of which the formation of two amine fragments occurs by cleavage of the same C—C bond, is lower by more than an order of magnitude than in the spectrum of analog XI. The fact that the peaks of ions with lower mass numbers that are formed in the cleavage of various bonds of the bicyclic system have very low intensities in the spectra of derivatives XII and XIV is noteworthy. For example, the spectra of XIV, which is characterized by a symmetrical structure relative to the exocyclic C—C bond, at 70 and 12 eV contain essentially only one peak (140), which corresponds to ion *l*. Thus, on the one hand, the stabilities of these compounds with respect to electron impact decrease, whereas, on the other, processes involving cleavage of the bonds in the bicyclic system are absent, and the resistance to further fragmentation of the amine fragments of the *l* or m type increases. This behavior of the compounds under electron impact can be explained by, first, equally probable ionization of the two equivalent nitrogen atoms and, second, the very low ionization potentials of the nitrogen atoms in alicyclic compounds [10]. The dissociation processes in the fragmentation of such compounds may therefore take place more rapidly than when a quasi-equilibrium state is established in the molecular ion [11]. Thus the rapid fragmentation of highly excited M^+ explains the low stabilities of these compounds with respect to electron impact, while the formation of ions *l* or m with a small reserve of internal energy is responsible for their stability with respect to further transformations. A more detailed study of such processes is of definite theoretical interest for the mass spectrometry of organic compounds.

Thus, as a result of this research, we have studied the peculiarities in the behavior of 3,9-diazabicyclo[3.3.1]nonanes and their oxygen analogs under electron impact as a function of their three-dimensional structures and the character of the substituents. We have shown that the intensities of the peaks of the characteristic fragments in the spectra of such compounds are determined by the properties of the ring heteroatoms and their mutual orientation relative to one another. The results of this research can be used to establish the structures of alicyclic amines and related compounds.

EXPERIMENTAL

Compounds I-XV were synthesized, purified, and kindly placed at our disposal by E. S. Nikit-skaya and co-workers. The synthesis of the compounds was published in [3, 12, 13].

The mass spectra were obtained with an LKB-9000 mass spectrometer with direct introduction of the samples into the ion source; the ionizing voltages were 12, 14, 30, and 70 eV, the temperature of the ionization chamber was 200-250°C, and the emission current was 60 μA.

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