11. Yu. A. Azev, I. Ya. Postovskii, E. L. Pidemskii, and A. F. Goleneva, Khim.-Farm. Zh., No. 4, 39 (1980).
12. S. Nishigaki, H. Kanazawa, Y. Kanamori, M. Ichiba, and K. Senga, J. Heterocycl. Chem., 19, 1309 (1982).
13. C. M. Atkinson and H. D. Cossey, J. Chem. Soc., No. 3, 1628 (1963).
14. G. Doleschall and K. Lempert, Acta Chim. Acad. Sci. Hung., 77, 345 (1973).
15. S. G. Alekseev, V. N. Charushin, O. N. Chupakhin, S. V. Shorshnev, A. I. Chernyshev, and N. A. Klyuev, Khim. Geterotsikl. Soedin., No. 11, 1535 (1986).
16. R. J. Pugmire and D. M. Grant, J. Am. Chem. Soc., 90, 697 (1968).
17. G. G. Dvoryantseva, T. Ya. Filipenko, I. S. Musatova, A. S. Elina, P. V. Petrovskii, E. V. Arshavskaya, and É. I. Fedin, Izv. Akad. Nauk SSSR, Ser. Khim., No. 5, 1060 (1977).
18. S. Ya. Mel'nik, A. A. Bakhmedova, Yu. Yu. Volodin, M. N. Preobrazhenskaya, A. I. Chernyshev, S. E. Esipov, and S. M. Navashin, Bioorg. Khim., No. 11, 1723 (1981).
19. R. J. Pugmire and D. M. Grant, J. Am. Chem. Soc., 93, 1880 (1971).
20. R. Drago, Physical Methods in Chemistry [Russian translation], Vol. 1, Mir, Moscow (1981), p. 333.
21. S. G. Alekseev, P. A. Torgashev, M. A. Fedotov, A. I. Rezvukhin, S. V. Shorshnev, A. V. Belik, V. N. Charushin, and O. N. Chupakhin, Khim. Geterotsikl. Soedin., No. 4, 525 (1988).
22. E. Breitmaier and W. Voelter, ^{13}C NMR Spectroscopy, Verlag Chemie, Weinheim–New York (1978), p. 82.
23. A. Gordon and R. Ford, The Chemist's Guide [Russian translation], Mir, Moscow (1976), p. 79.

MASS-SPECTROMETRIC STUDY OF THE PRODUCTS OF INTRAMOLECULAR CYCLIZATION OF 1,3-AMIDO ALCOHOLS. 5-6-DIHYDRO-4H-1,3-OXAZINES AND 2-OXAZOLINES

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The mass spectra of substituted 5,6-dihydro-4H-1,3-oxazines and 2-oxazolines were studied for the identification of the products of intramolecular cyclization of 1,3-amido alcohols. The fragmentation of the molecular ions of 1,3-oxazines under the influence of electron impact proceeds via both fragmentation of the retrodiene type and with the formation of rearrangement ions, the relative intensities of the peaks of which are determined by the nature and position of the substituents in the heteroring. The molecular ions of 2-oxazolines undergo fragmentation chiefly with the loss of a molecule of a ketone.

One of the most widely used methods for the synthesis of 5,6-dihydro-4H-1,3-oxazines is the intramolecular cyclization of 1,3-amido alcohols under the influence of concentrated sulfuric acid [1]. However, it was recently established that the formation of both 5,6-dihydro-4H-1,3-oxazines and 2-oxazolines or mixtures of both isomeric cyclic imino esters is possible during this reaction, depending on the structure of the starting 1,3-amido alcohol [2, 3]. The closeness of the ^{1}H and ^{13}C NMR spectra of these compounds often makes it possible to draw an unambiguous conclusion regarding their structures. The analysis of the parameters of the NMR spectra of mixtures of both possible cyclic imino esters is fraught with

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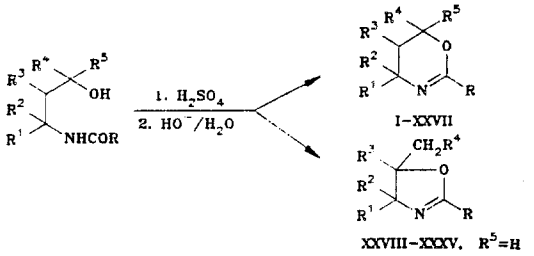
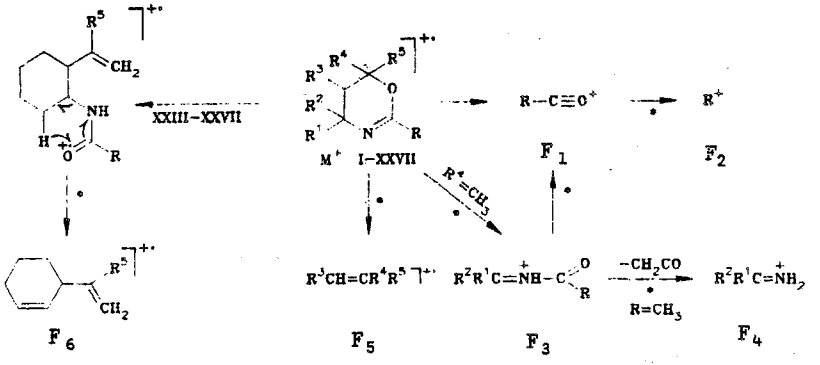
even greater difficulties. The problem of the choice between the two isomeric structures can be solved to a great extent by using mass spectrometry. The need for the present research was also due to the scantiness of the literature data on the mass-spectral behavior of such compounds, of which only 2-phenyl-4,5-dihydro-1,3-oxazin-6-ones [4] and 2-aryl-5,6-dihydro-1,3-oxazin-5-ones [5, 6] have been studied; their fragmentation under the influence of electron impact was found to depend to a considerable extent on the position of the carbonyl group in the heteroring.

In order to find reliable characteristics for establishing the structures of isomeric 5,6-dihydro-4H-1,3-oxazines and 2-oxazolines we studied the mass spectra of I-XXVII and XXVIII-XXXV, which were assigned by means of other methods or on the basis of their synthesis [2, 3, 7] to the 1,3-oxazine and 2-oxazoline groups, respectively.



An analysis of the mass-spectral data (Tables 1-3) shows that the differences in the stabilities with respect to electron impact of the molecular ions M^+ of I-XXVII (W_M = 0.5-9.9%) and XXVIII-XXXV (W_M = 0.5-4.0%) are insignificant and that the W_M value therefore cannot serve as an analytical characteristic of their mass-spectral behavior. At the same time, as expected, a number of substantial differences are observed in the fragmentation of the M^+ ions of I-XXVII and XXVIII-XXXV.

Scheme 1



With respect to the character of the fragmentation of the M^+ ions, monocyclic 5,6-dihydro-1,3-oxazines I-XIX can be divided into four groups (Table 2, Scheme 1). For 2-phenyl-substituted 1,3-oxazines VII and VIII, which do not contain a substituent attached to the $C_{(6)}$ atom of the heteroring and were assigned to the first group, the principal peak in the spectrum is the peak of the benzoyl cation (F_1) with m/z 105. The peak of ion also has the maximum intensity in the spectra of 1,3-oxazines IX-XII with an alkyl substituent attached to the $C_{(6)}$ atom of the heteroring, which constitute the second group of compounds. However, also characteristic for these compounds is fragmentation of the M^+ ion with the formation of rearrangement fragment F_3 as a result of migration of a hydrogen atom from the methyl group attached to the $C_{(6)}$ atom of the heteroring through the six-membered transition state to the nitrogen atom and the detachment of a hydrocarbon radical. In the case of 2-methyl-substituted 1,3-oxazines I-III, which constitute the third group of compounds, fragmentation of the F_3 fragment with the loss of a molecule of ketene leads to the formation of amino fragment F_4, the peak of which has the maximum intensity in the spectrum. The fourth group of compounds is made up of 1,3-oxazines IV-VI and XIII-XIX with a phenyl substituent attached to the $C_{(6)}$ atom of the heteroring, in the spectra of which the principal peak corresponds to alkenylbenzene ion F_5, which is formed as a result of retrodiene fragmentation of the M^+ ion. The subsequent fragmentation of the F_5 ion proceeds via the usual scheme of the fragmentation of alkenylbenzenes [8]: the elimination of a molecule of

TABLE 1. Mass Spectra of I-XXXV*

Compound	m/z (relative intensity, %)
1	2
I	141 (35), 126 (7), 101 (11), 100 (42), 58 (100), 57 (7), 43 (40), 42 (22), 41 (16), 39 (8)
II	155 (5), 100 (39), 72 (10), 70 (9), 60 (15), 58 (100), 55 (13), 43 (59), 42 (21), 41 (20), 39 (7)
III	155 (13), 100 (78), 99 (25), 96 (21), 60 (70), 59 (43), 58 (100), 57 (21), 43 (67), 42 (8), 41 (23)
IV	189 (11), 118 (100), 117 (32), 105 (26), 103 (28), 91 (28), 78 (25), 77 (63), 51 (35), 43 (75), 42 (45)
V	217 (3), 119 (11), 118 (100), 117 (14), 115 (29), 105 (17), 100 (40), 77 (16), 58 (82), 43 (93), 42 (15)
VI	175 (13), 132 (14), 105 (15), 104 (100), 84 (14), 78 (24), 77 (23), 69 (19), 43 (47), 42 (35), 41 (20)
VII	161 (38), 160 (28), 106 (8), 105 (100), 104 (9), 103 (25), 77 (65), 76 (12), 51 (25), 50 (9), 39 (7)
VIII	189 (19), 174 (8), 106 (7), 105 (100), 77 (27), 70 (10), 51 (11), 55 (8), 44 (8), 43 (14), 41 (15)
IX	189 (25), 134 (34), 106 (7), 105 (100), 104 (16), 77 (40), 56 (17), 51 (12), 43 (9), 41 (19), 39 (8)
X	203 (18), 188 (9), 106 (11), 105 (100), 104 (7), 103 (5), 77 (29), 56 (5), 51 (8), 43 (10), 41 (12)
XI	217 (10), 162 (23), 106 (8), 105 (100), 104 (7), 77 (33), 55 (7), 51 (7), 43 (8), 41 (11), 39 (5)
XII	217 (10), 162 (19), 106 (8), 105 (100), 77 (23), 71 (8), 69 (12), 56 (10), 55 (7), 43 (23), 41 (21)
XIII	251 (23), 118 (100), 117 (31), 105 (70), 104 (18), 103 (46), 91 (20), 78 (25), 77 (74), 51 (35), 43 (31)
XIV	279 (5), 162 (16), 119 (11), 118 (100), 117 (21), 105 (83), 103 (14), 78 (14), 77 (60), 51 (12), 43 (11)
XV	237 (18), 105 (60), 104 (100), 103 (39), 78 (32), 77 (84), 76 (12), 51 (34), 50 (9), 43 (10), 39 (10)
XVI	251 (31), 119 (10), 118 (100), 117 (40), 105 (47), 104 (22), 91 (9), 77 (24), 51 (7), 43 (12), 41 (7)
XVII	313 (15), 193 (6), 106 (6), 105 (80), 104 (100), 103 (14), 91 (9), 78 (24), 77 (75), 51 (15), 39 (4)
XVIII	313 (3), 180 (100), 179 (34), 178 (22), 165 (18), 105 (44), 104 (64), 103 (17), 78 (23), 77 (54), 51 (16)
XIX	313 (31), 192 (17), 181 (20), 180 (100), 178 (22), 166 (6), 165 (41), 105 (46), 103 (16), 77 (45), 51 (9)
XX	221 (14), 162 (14), 140 (95), 98 (100), 81 (20), 79 (13), 67 (21), 55 (14), 54 (17), 43 (88), 41 (34)
XXI	215 (27), 134 (57), 105 (100), 104 (13), 77 (45), 67 (29), 55 (11), 54 (17), 51 (12), 41 (25), 39 (14)
XXII	229 (14), 149 (6), 148 (59), 106 (7), 105 (100), 77 (26), 67 (13), 55 (11), 54 (6), 43 (6), 41 (10)
XXIII	229 (20), 106 (7), 105 (100), 104 (7), 77 (47), 67 (8), 55 (11), 51 (10), 43 (12), 41 (14), 39 (8)
XXIV	243 (27), 122 (71), 107 (16), 105 (100), 95 (9), 77 (36), 69 (14), 57 (16), 55 (16), 43 (29), 41 (25)
XXV	246 (28), 125 (54), 124 (17), 122 (16), 106 (10), 105 (100), 77 (39), 45 (9), 44 (13), 43 (15), 41 (11)
XXVI	257 (17), 136 (66), 122 (19), 121 (8), 107 (28), 106 (9), 105 (100), 77 (30), 55 (9), 43 (15), 41 (12)
XXVII	305 (26), 184 (70), 169 (51), 105 (100), 104 (16), 91 (13), 77 (54), 55 (14), 44 (13), 43 (23), 41 (19)
XXVIII	127 (9), 98 (33), 73 (16), 70 (19), 69 (11), 57 (18), 55 (100), 54 (15), 43 (38), 42 (17), 39 (9)
XXIX	141 (12), 84 (25), 70 (33), 69 (100), 58 (33), 57 (23), 56 (30), 55 (55), 43 (55), 42 (48), 41 (40)
XXX	181 (1), 84 (8), 83 (100), 79 (4), 69 (4), 58 (10), 55 (10), 43 (20), 42 (85), 41 (26), 39 (10)
XXXI	221 (4), 124 (10), 123 (100), 82 (13), 81 (8), 67 (40), 55 (8), 54 (11), 43 (14), 42 (8), 41 (15)
XXXII	189 (13), 160 (10), 117 (100), 105 (22), 77 (37), 57 (26), 55 (21), 51 (17), 43 (31), 42 (11), 41 (28)
XXXIII	215 (16), 158 (9), 118 (21), 117 (100), 105 (31), 90 (11), 55 (16), 51 (14), 43 (18), 41 (28), 39 (12)
XXXIV	229 (6), 132 (21), 131 (100), 130 (34), 105 (21), 104 (28), 103 (44), 77 (35), 55 (24), 42 (11), 41 (24)
XXXV	283 (18), 185 (100), 105 (47), 104 (41), 82 (29), 77 (32), 67 (73), 54 (21), 43 (40), 42 (30), 41 (30)

*The peaks of the M^+ ions and the 10 most intense ion peaks in the mass spectra are presented.

TABLE 2. Intensities of the Peaks of the Characteristic Ions in the Mass Spectra of I-XXVII (% Σ_{39})

Compound	Substituent						Fragment						
	R	R^1	R^2	R^3	R^4	R^5	W_M	F_1	F_2	F_3	F_4	F_5	F_6
I	CH_3	CH_3	CH_3	H	CH_3	H	9,9	10,2	—	10,7	25,5	5,6	—
II	CH_3	CH_3	CH_3	CH_3	CH_3	H	1,4	15,3	—	10,2	25,9	1,8	—
III	CH_3	CH_3	CH_3	H	CH_3	CH_3	2,2	10,5	—	12,3	15,8	2,8	—
IV	CH_3	H	H	H	CH_3	C_6H_5	1,7	10,2	—	0,8	4,1	13,6	—
V	CH_3	CH_3	CH_3	H	CH_3	C_6H_5	0,6	13,6	—	5,8	12,0	14,6	—
VI	CH_3	H	H	H	H	C_6H_5	3,0	9,3	—	—	—	20,0	—
VII	C_6H_5	H	H	H	H	H	9,7	23,0	15,0	—	—	3,5	—
VIII	C_6H_5	CH_3	CH_3	H	H	H	5,7	27,0	7,3	—	—	4,4	—
IX	C_6H_5	H	H	CH_3	CH_3	H	4,7	16,3	6,6	5,6	—	2,8	—
X	C_6H_5	CH_3	CH_3	H	CH_3	H	5,9	28,4	8,2	0,5	—	1,0	—
XI	C_6H_5	CH_3	CH_3	CH_3	CH_3	H	3,9	34,8	11,5	8,1	—	1,3	—
XII	C_6H_5	CH_3	CH_3	H	CH_3	CH_3	2,9	23,6	5,5	4,6	—	2,3	—
XIII	C_6H_5	H	H	H	CH_3	C_6H_5	3,7	9,6	10,0	0,8	—	13,6	—
XIV	C_6H_5	CH_3	CH_3	H	CH_3	C_6H_5	1,2	16,6	12,0	3,3	—	20,0	—
XV	C_6H_5	H	H	H	H	C_6H_5	3,9	11,0	15,5	—	—	18,4	—
XVI	C_6H_5	H	H	CH_3	H	C_6H_5	8,5	10,6	5,3	—	—	22,6	—
XVII	C_6H_5	H	C_6H_5	H	H	C_6H_5	4,2	18,2	17,0	—	—	22,6	—
XVIII	C_6H_5	H	H	C_6H_5	H	C_6H_5	0,5	8,2	10,0	—	—	18,5	—
XIX	C_6H_5	H	H	H	C_6H_5	C_6H_5	8,2	9,0	8,7	—	—	19,4	—
XX	CH_3	$-(CH_2)_5-$		$-(CH_2)_4-$		H	2,3	12,3	—	13,3	14,0	1,4	—
XXI	C_6H_5	H	H	$-(CH_2)_4-$		H	6,2	19,8	9,0	11,3	—	1,0	—
XXII	C_6H_5	H	CH_3	$-(CH_2)_4-$		H	4,3	26,3	6,8	15,6	—	1,4	—
XXIII	C_6H_5	H	$-(CH_2)_4-$		CH_3	H	5,3	23,5	11,0	—	—	—	1,6
XXIV	C_6H_5	H	$-(CH_2)_4-$		CH_3	CH_3	5,2	16,4	5,9	—	—	—	8,7
XXV	C_6H_5	H	$-(CH_2)_4-$		CH_3	CD_3	6,2	19,0	7,4	—	—	—	10,5
XXVI	C_6H_5	H	$-(CH_2)_4-$		CH_3	C_2H_5	4,4	21,2	6,3	—	—	—	14,0
XXVII	C_6H_5	H	$-(CH_2)_4-$		CH_3	C_6H_5	4,3	13,6	7,3	—	—	—	9,5

TABLE 3. Intensities of the Peaks of the Characteristic Ions in the Mass Spectra of XXVIII-XXXV (% Σ_{39})

Compound	Substituent					Fragment				
	R	R^1	R^2	R^3	R^4	W_M	F_1	F_2	F_7	F_8
XXVIII	CH_3	H	H	CH_3	CH_3	1,9	7,0	—	18,3	6,1
XXIX	CH_3	CH_3	H	CH_3	CH_3	2,0	7,5	—	13,5	1,2
XXX	CH_3	CH_3	CH_3	$-(CH_2)_4-$		0,5	5,9	—	28,4	—
XXXI	CH_3	$-(CH_2)_5-$		$-(CH_2)_4-$		1,3	4,1	—	29,5	—
XXXII	C_6H_5	H	H	CH_3	CH_3	2,7	3,9	6,4	17,6	1,8
XXXIII	C_6H_5	H	H	$-(CH_2)_4-$		4,0	6,2	0,6	20,2	—
XXXIV	C_6H_5	CH_3	H	$-(CH_2)_4-$		1,4	3,9	6,7	19,0	—
XXXV	C_6H_5	$-(CH_2)_5-$		$-(CH_2)_4-$		2,8	5,8	4,0	12,2	—

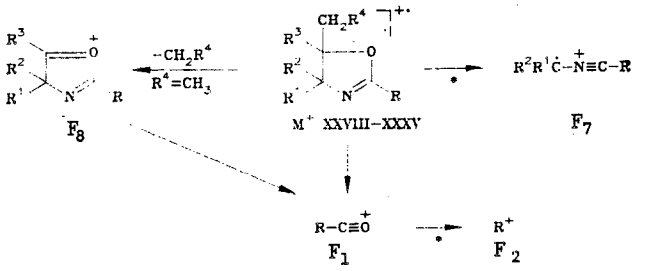
acetylene ($R^3 = R^4 = H$) and the successive detachment of a hydrogen atom and a molecule of acetylene (R^3, $R^4 = H$, CH_3) or the loss of a methyl radical (R^3, $R^4 = C_6H_5$).

The peak of benzoyl cation F_1 also has the maximum intensity in the spectra of 5,6- and 4,5-tetramethylene-substituted 1,3-oxazines (XXI, XXII, and XXIII-XXVII, respectively). However, whereas the fragmentation of the M^+ ions of XX-XXII (Scheme 1, Table 2) proceeds via pathways involving the fragmentation of the M^+ ions of 6-alkyl-substituted 5,6-dihydro-1,3-oxazines (for example, the formation of F_3 and F_5 fragments), such processes in the fragmentation of the M^+ ions are not characteristic for XXIII-XXVII. The presence of peaks of hydrocarbon fragments F_6, which are formed as a result of the migration of two hydrogen atoms to the ring nitrogen and oxygen atoms and the subsequent detachment of an RC(OH)NH molecule from the M^+ ion (Scheme 1), is more likely for the mass spectra of XXIII-XXVII. This difference in the character of the fragmentation of the M^+ ions makes it possible to easily determine the site of fusion of the hydrocarbon and 1,3-oxazine rings in XX-XXII and XXIII-XXVII.

The mass spectra of 2-oxazolines XXVIII-XXXV (Table 3) also contain peaks of F_1 fragments, although their intensities are somewhat lower than the intensities of the peaks of the analogous ions in the spectra of I-XXVII. As in the previously studied substituted imidazolines [9], 2-oxazolines [10], and 2-thiazolines [11], the principal pathway in the

fragmentation of the M^+ ions of XXVIII-XXXV (Scheme 2) is associated with the initial cleavage of the $C_{(2)}$–O bond and subsequent detachment of a ketone molecule (the F_7 fragment). Detachment of an ethyl radical from the M^+ ion with the formation of an F_8 fragment is also characteristic for XXVIII, XXIX, and XXXII.

Scheme 2



The above-presented schemes of the processes involved in the dissociative ionization of I-XXXV are confirmed by the presence in their mass spectra of peaks of the corresponding metastable ions (in Schemes 1 and 2 these fragmentation pathways are denoted by asterisks).

Thus, the presence of intense peaks of F_1, F_3, and F_5 ions in the mass spectrum makes it possible to assume an oxazine structure of the compound. On the other hand, the absence of peaks of F_3 and F_5 ions in the spectra and high intensities of the peaks of F_7 ions indicate the presence of an oxazoline structure of the compound.

EXPERIMENTAL

The mass spectra of I-XXXV were obtained with a Varian model MAT CH-6 spectrometer at an ionizing-electron energy of 70 eV and a cathode emission current of 100 μA. The samples were introduced into the ion source by the direct-introduction technique. The temperature of the admission system was 20-35°C.

The synthesis of the investigated I-XXXV was previously described in [2, 3, 7].

LITERATURE CITED

1. Z. Eckstein and T. Urbanski, Adv. Heterocycl. Chem., 23, 1 (1978).
2. A. P. Guzaev, I. P. Boiko, Yu. F. Malina, and B. V. Unkovskii, Ref. Zh. Khim., 4Zh276 (1983).
3. A. P. Guzaev, A. B. Khasirdzhev, M. M. Borunov, Yu. F. Malina, A. U. Stepanyants, and B. V. Unkovskii, Ref. Zh. Khim., 4Zh275 (1983).
4. P. B. Terent'ev, Khr. Ivanov, and A. Dobrev, Khim. Geterotsikl. Soedin., No. 12, 1627 (1980).
5. P. A. Sharbatyan, A. T. Lebedev, V. G. Kartsev, and A. M. Sipyagin, Khim. Geterotsikl. Soedin., No. 1, 43 (1981).
6. A. T. Lebedev, P. A. Sharbatyan, A. M. Sipyagin, V. G. Kartsev, and V. S. Petrosyan, Khim. Geterotsikl. Soedin., No. 10, 1332 (1983).
7. C. Giordano, G. Ribaldone, and G. Borsotti, Synthesis, No. 2, 92 (1971).
8. V. V. Takhistov, The Practical Mass Spectrometry of Organic Compounds [in Russian], Izd. Leningradsk. Gosudarstv. Univ., Leningrad (1977).
9. M. Ohashi, N. Ohno, H. Kakisawa, A. Tatematsu, and H. Yoshizumi, Org. Mass Spectrom., 1, 703 (1968).
10. R. T. Lundquist and A. Ruby, Appl. Spectrosc., 20, 258 (1966).
11. J. Linares, E.-J. Vincent, and G. Salmona, Org. Mass Spectrom., 11, 873 (1976).