MASS-SPECTROMETRIC IDENTIFICATION OF ISOMERIC 1-BENZOYL-2-AZETIDINONES AND 2-PHENYL-4,5-DIHYDRO-1,3-OXAZIN-6-ONES

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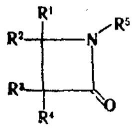
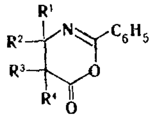
The mass spectra of isomeric 1-benzoyl-2-azetidinones and 2-phenyl-4,5-dihydro-1,3-oxazin-6-ones were analyzed. A more stable molecular ion and high intensities of the peaks of the ions formed from the molecular ion with the loss of ketene or a substituted ketene are characteristic for the former compounds, while low stability of the molecular ion and a higher probability of the loss of one of the groupings in the 4 position are characteristic for the latter compounds. Fragmentation schemes that are confirmed by the high-resolution mass spectra are presented.

The cyclization of 3-benzamidopropionic acids under the influence of acetic anhydride leads to the formation of both 4,5-dihydro-1,3-oxazin-6-ones [1-3] and 1-benzoyl-2-azetidinones [4, 5]. The closeness of the IR spectra of these compounds often does not make it possible to draw an unambiguous conclusion regarding their structures [6, 7]. In [8] it was assumed that the presence in the mass spectrum of an intense ion peak of an olefin fragment constitutes evidence for an azetidinone structure for the compound. However, this conclusion was drawn on the basis of an analysis of the mass spectra of only four compounds and was not sufficiently convincing.

In order to find more reliable characteristics to establish the structures of such isomeric compounds we studied the mass spectral behavior of two series of compounds (I-XIX):



I-X



XI-XIX

	R¹	R²	R³	R⁴	R⁵
I	CH_3	CH_3	H	H	C_6H_5CO
II	C_6H_5	C_6H_5	C_6H_5	H	C_6H_5CO
III	C_6H_5	CH_3	CH_3	CH_3	C_6H_5CO
IV	C_6H_5	C_6H_5	CH_3	CH_3	C_6H_5CO
V	$-CH(CH_3)-(CH_2)_4-$		H	H	C_6H_5CO
VI	$-CH_2-CH(CH_3)-(CH_2)_3-$		H	H	C_6H_5CO
VII	C_6H_5	C_6H_5	$-(CH_2)_5-$		C_6H_5CO
VIII	$-CH_2-C(CH_3)_2-CH_2-C(CH_3)_2-CH_2-$		H	H	C_6H_5CO
IX	C_6H_5	CH_3	CH_3	H	C_6H_5
X	C_6H_5	H	$-(CH_2)_5-$		C_6H_5
XI	C_6H_5	C_6H_5	H	H	—
XII	CH_3	CH_3	H	H	—
XIII	CH_3	C_2H_5	H	H	—
XIV	C_3H_7	C_3H_7	H	H	—
XV	$-(CH_2)_5-$		H	H	—
XVI	$-(CH_2)_6-$		H	H	—
XVII	$-(CH_2)_5-$		CH_3	H	—
XVIII	$-(CH_2)_5-$		CH_3	CH_3	—
XIX	H	$-(CH_2)_4-$		H	—

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TABLE 1. Mass Spectra of I-XIX

Compound	m/e (relative intensity, %)[a]
I	203 (26), 188 (3), 148 (52), 105 (100), 77 (48), 76 (3), 56 (59), 51 (14), 50 (4), 41 (10), 39 (4)
II	403 (37), 287 (20), 286 (56), 256 (15), 178 (14), 165 ([illegible]), 118 (100), 105 (72), 103 (8), 90 (28), 77 (37)
III	293 (33), 225 (20), 224 (70), 190 (8), 131 (2), 105 (100), 103 (3), 77 (22), 70 (19), 51 (2), 42 (3)
IV	355 (26), 286 (57), 208 (3), 165 (8), 105 (100), 91 (7), 77 (93), 70 (33), 51 (13), 42 (24), 41 (12)
V	257 (21), 256 (5), 242 (4), 105 (100), 77 (87), 69 (18), 57 (12), 55 (16), 51 (7), 43 (24), 42 (26)
VI	257 (18), 229 (18), 215 (7), 214 (14), 201 (6), 136 (9), 122 (17), 108 (10), 105 (100), 77 (37), 51 (5)
VII	395 (20), 287 (18), 286 (75), 165 (4), 122 (17), 110 (11), 105 (100), 77 (24), 67 (11), 57 (8), 43 (7)
VIII	299 (33), 284 (19), 242 (20), 178 (18), 163 (50), 137 (53), 136 (20), 135 (20), 132 (15), 105 (100), 77 (33)
IX	251 (39), 182 (12), 181 (78), 180 (34), 132 (100), 131 (6), 117 (44), 104 (7), 91 (10), 77 (25), 51 (7)
X	291 (36), 182 (22), 181 (100), 180 (25), 172 (39), 129 (7), 115 (4), 101 (17), 91 (11), 81 (24), 77 (16)
XI	327 (3), 299 (5), 194 (5), 180 (25), 179 (7), 178 (8), 105 (100), 103 (12), 77 (69), 51 (20), 42 (10)
XII	203 (9), 188 (8), 105 (100), 104 (14), 103 (3), 77 (58), 76 (8), 56 (28), 51 (17), 42 (16), 41 (12)
XIII	217 (2), 188 (46), 105 (100), 104 (5); 77 (43), 76 (4), 70 (11), 55 (11), 51 (13), 42 (8), 41 (5)
XIV	259 (1), 231 (5), 216 (32), 189 (5), 188 (6), 138 (7), 105 (100), 77 (40), 56 (5), 51 (8), 43 (5)
XV	243 (5), 215 (5), 200 (2), 187 (2), 122 (6), 105 (100), 96 (2), 81 (4), 77 (36), 43 (3), 41 (3)
XVI	257 (3), 229 (31), 201 (10), 200 (9), 186 (9), 136 (7), 122 (14), 105 (100), 77 (47), 51 (7), 41 (7)
XVII	257 (3), 229 (2), 202 (3), 105 (100), 103 (5), 77 (78), 56 (52), 55 (31), 51 (5), 42 (5), 41 (38)
XVIII	271 (1), 202 (43), 168 (17), 105 (100), 81 (10), 77 (60), 70 (70), 55 (6), 51 (6), 42 (20), 41 (27)
XIX	229 (10), 139 (9), 125 (10), 122 (15), 105 (100), 96 (14) 82 (17), 77 (45), 67 (14), 56 (10), 43 (45)

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[a] The molecular ions and the 10 most intense peaks are presented. The peaks of the isotopic ions are not presented.

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

Compound	W_M	F_1	F_{1+H}	F_{1-H}	F_2	F_3	F_4	F_5	F_6	F_7	m/e 105	m/e 77
I	7,2	—	—	—	0,6	16,0	—	0,1	1,9	0,9	27,2	13,0
II	8,0	—	8,6	—	15,6	2,3	0,6	—	0,2	—	11,0	5,6
III	13,2	—	24,0	—	6,2	0,5	—	—	—	—	36,0	7,2
IV	7,2	—	13,3	—	7,7	0,6	0,7	—	0,4	—	23,1	21,6
V	6,0	—	—	0,1	—	—	—	—	—	—	26,8	23,2
VI	6,8	2,4	—	4,6	—	0,9[a]	—	6,1	0,5	—	34,7	13,0
VII	6,5	—	23,6	—	3,5	1,0	0,8	—	—	—	31,7	7,8
VIII	8,2	0,2	—	0,6	—	—	—	2,8	—	—	20,8	6,8
IX	9,5	27,2	1,9	—	—	24,8	4,7	—	—	—	—	6,2
X	9,6	19,3	—	6,8	—	10,6	1,6	—	—	—	—	4,4
XI	1,1	0,1	0,1	—	3,2	—	8,1	1,6	1,5	0,3	60,0	22,4
XII	2,3	0,2	0,4	0,2	4,4	—	7,6[a]	0,3	—	2,7	27,2	15,7
XIII	0,7	—	—	—	2,9	—	4,2[a]	2,2	—	17,8	39,8	17,0
XIV	0,4	—	—	—	1,0	0,9[a]	—	1,8	—	12,2	37,8	15,0
XV	2,5	0,3	—	3,7	1,6	0,9	0,3	9,6	0,3	2,1	19,8	14,1
XVI	1,0	0,6	—	0,8	0,4	0,8	—	9,1	—	5,4[b]	29,5	13,7
XVIII	0,9	—	0,9	—	14,8	0,1	—	0,7	0,3	1,4[c]	28,4	22,3
XVIII	0,2	0,5	—	—	17,5	0,4	—	—	0,1	10,8[a]	25,3	15,2
XIX	1,9	—	—	—	—	0,9	—	2,5	3,5	—	24,6	11,1

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[a] On the basis of the high-resolution mass spectra.

[b] M—C_4H_8.

[c] M—C_5H_{10}.

Some of them have already been classified as azetidinones (II, X, and XI) or oxazinones (XII-XIV) by means of other methods (or on the basis of the synthetic method). The literature contains no unified opinion relative to the structure of the remaining compounds. The mass spectra of the substances that we investigated are presented in Table 1, while the relative intensities of the peaks of some characteristic ions are given in Table 2.

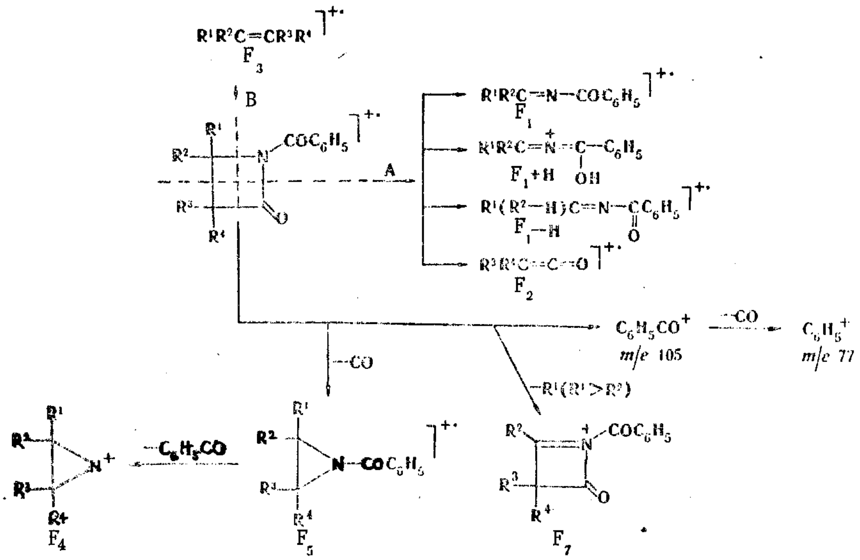
An analysis of the data obtained show that, in analogy with the conclusion in [8], the character of the dissociative ionization is similar for all of the investigated compounds (Schemes 1 and 2).

In most cases (except for II, IX, and X) the maximum peak in the mass spectrum corresponds to the benzoyl cation with m/e 105, while the peak of the phenyl cation with m/e has the second highest intensity. The percentages of these two ions in the total ion current often reaches 40-60% (see Table 2).

An analysis of the intensities of the peaks of the molecular and other fragment ions of the investigated compounds shows that the molecular ions of I-X are relatively stable (W_M = 6-13%), while the stabilities of the molecular ions of XI-XIX are appreciably lower (W_M = 0.2-2.9%).

Intense peaks of F_1, (F_1 + H), or (F_1 − H) are characteristic in most cases for the mass spectra of the compounds of the first group. These ions are formed by cleavage of the ring via pathway A (Scheme 1), which is characteristic for the dissociative ionization of derivatives of 1-substituted 2-azetidinones [9-12] and unsubstituted 2-azetidinones [13]. On the other hand, in the mass spectra of compounds of the second group these ions are either absent or the intensities of their peaks are insignificant.

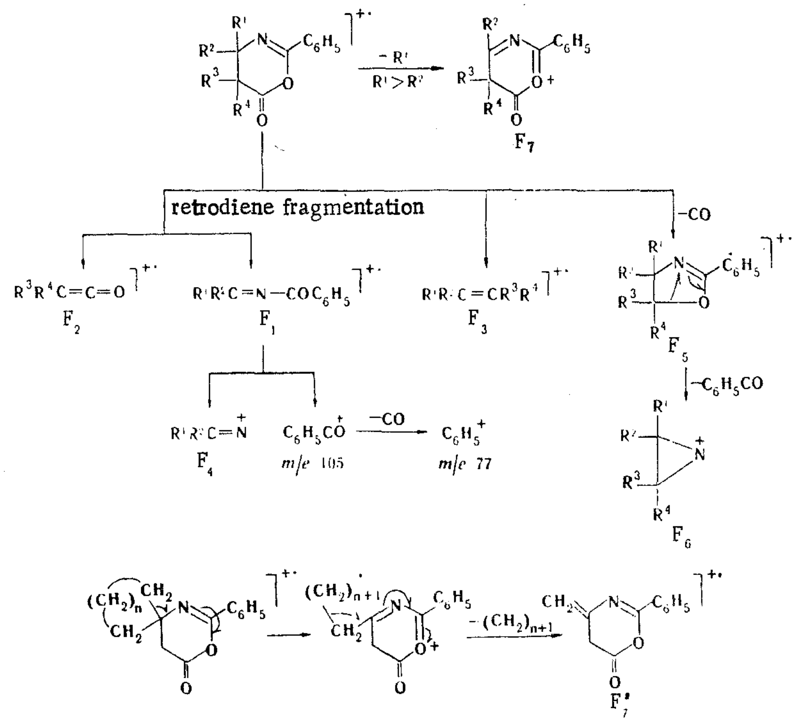
Scheme 1



An intense peak of an olefin fragment (F_3 for I, IX, and X), which is formed by cleavage via pathway B, is actually observed in the mass spectra of some compounds of the first group; however, this is not the rule. A low-intensity ion peak with a similar structure is observed in the mass spectra of many compounds of both groups. Let us also note that according to the data from the high-resolution mass spectra, such ions (F_3) are often isobaric with respect to the F_4 fragments (XI-XIII). Thus the presence or absence of an F_3 (F_4) olefin fragment cannot be regarded as a sufficiently conclusive sign of the affiliation of an analyzed compound with the azetidinone or oxazinone group. One observes F_2, F_5, and F_6 ions in the mass spectra of compounds of both groups, and they probably cannot characterize a definite structure. It follows from the data in Table 2 that the presence of a rather intense peak of an F_7 ion, which is formed due to elimination from the molecular ion of an R^1 grouping (when $R^1>R^2$) in the α position relative to the ring nitrogen atom, is characteristic for all compounds of the second group (XI-XIX) (Scheme 2).

In the case of spiro compounds (XV-XVIII), after cleavage of the same C—C bond, one observes splitting out of an olefin with the formation of an F_7' (see display after Scheme 2):

Scheme 2



These data make it possible to regard the presence of an intense F_7 (F_7') ion peak as one of the rather reliable signs of the existence of a six-membered oxazinone structure. Both F_1, $F_1 + H$, and F_1-H ions and the F_7 ion were absent only in the mass spectrum of XIX. However, the low stability of its molecular ion made it possible to assume the existence of a six-membered heteroring. An additional confirmation of this is the presence in the mass spectrum of the peak of an ion with m/e 185 ($[M-CO_2]^+$), the formation of which from the molecular ion was confirmed by the peak of a metastable ion with an apparent mass of 149.1 (calculated value 149.2).

Thus the relatively high stability of the molecular ion (W_M greater than 6.0%) with respect to electron impact and the presence in the mass spectrum of intense peaks of F_1, (F_1 + H), or (F_1-H) ions make it possible to propose an azetidinone structure for the compound. On the other hand, the stability of the molecular ion ($W_M<3.0$), the low intensity of the peaks of the F_1 (F_1 + H), or (F_1-H) ions, and the high intensity of the peaks of the F_7 ions indicate the existence of the heterocyclic oxazinone system.

EXPERIMENTAL

The mass spectra were recorded with MKh-1303 (USSR), MAT-111 (Varian), and JMS-01-SG-2 (Jeol, Japan) spectrometers at ionizing-electron energies of, respectively, 50, 80, and 75 eV with direct introduction of the substances into the ion source. The mass spectra recorded with the same apparatus were reproduced with an accuracy of 5-10 relative percent, while the data obtained with different spectrometers differed by no more than 20-25 relative percent. The mass spectra of IX and X were in agreement with those in [11, 12] with an accuracy of up to 10%. The elementary compositions of the ions were determined with a JMS-01-SG-2 spectrometer under double-focusing conditions with recording of the mass spectra on a photoplate and automatic processing of the data.

The synthesis of the investigated compounds was described by one of us in [4, 5].

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REACTIVITIES OF HETEROCYCLIC COMPOUNDS IN NITRATION. 5.* KINETICS OF NITRATION OF 5-SUBSTITUTED 2-PICRYLAMINOPYRIDINES

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The kinetics of nitration of 5-bromo-, 5-chloro-, and 5-nitro-2-picrylaminopyridines in 80-96% sulfuric acid were studied by a spectrophotometric method. The kinetic parameters of nitration were calculated. The UV spectra of the neutral and protonated forms in aqueous sulfuric acid solutions were identified. It was established that the indicated compounds are nitrated in the protonated form. The relative (as compared with benzene) rates of nitration were calculated.

The kinetics of nitration of polynuclear pyridine-containing compounds have not yet been studied systematically. The literature contains only a report regarding the study of the reactivity of 2-picrylaminopyridine [1]. In the present research we investigated the kinetics of the nitration of 5-nitro-, 5-chloro-, and 5-bromo-substituted 2-picrylaminopyridines in sulfuric acid.

3-Nitro derivatives are formed in close-to-quantitative yields in the nitration of nitro-, chloro-, and bromo-substituted 2-picrylaminopyridines with a 15-20-fold excess of concentrated nitric acid in 95% sulfuric acid (H_2SO_4:HNO = 90:10) at 40-70°C:

R Cl, Br, NO_2

The nitration of the iodo derivative at 60°C terminates with the formation of 5-nitro-2-picrylaminopyridine when an equimolar amount of HNO_3 is used and with the formation of 3,5-dinitro-2-picrylaminopyridine when a 15-20-fold excess of HNO_3 is used. This constitutes evidence for a reaction that proceeds in accordance with the scheme (see scheme after Table 2 at top of next page):

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*See [1] for communication 4.

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