MASS-SPECTROMETRIC STUDY OF 5,6-DIHYDRO-4H-1,3-OXAZIN-5-ONES

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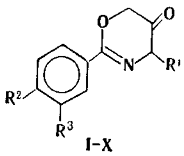
Under the influence of electron impact, 2-aryl-1,3-oxazin-5-ones undergo fragmentation primarily with the elimination of the $C_2H_2O_2$ group of atoms, as well as with the formation of aroyl cations. The complete absence of the retrodiene fragmentation that is characteristic for such heterocyclic systems makes it possible to conclude that, the double bond in the heteroring is not stabilized. In the case of 4-alkyl- and 4-benzyl-substituted oxazinones the molecular ions undergo rearrangement, as a result of which a seven-membered heteroring is formed due to inclusion of the methylene group of the substituent in an oxazine ring.

The reaction of 1-diazo-3-aroylaminopropan-2-ones with concentrated sulfuric acid yields 2-aryl-5,6-dihydro-4H-1,3-oxazin-5-ones, which constitutes a new type of previously uninvestigated heterocyclic system. These compounds were characterized by the IR, UV, and PMR spectra [1]. In the present research we investigated oxazinones I-X by mass spectrometry.



I-X

I—VI R^1=H; VII R^1=CH_3; VIII R^1=C_2H_5; IX, X R^1=$CH_2C_6H_5$; I, VII—IX R^2=H; II R^2=CH_3; III R^2=Cl; IV R^2=Br; V R^2=NO_2; VI, X R^2=R^3=OCH_3; I—V, VII—IX R^3=H

Molecular ion (M^+) peaks of very low intensity are observed in the mass spectra of all of the investigated compounds, and this constitutes evidence for the low stability of the molecules with respect to electron impact. Compound VI, in which two electron-donor methoxy groups stabilize M^+, has the highest W_M value (10.7, see Table 1). When the hydrogen atom in the 4 position is replaced by an alkyl or benzyl group, the W_M values become even lower; this is determined by the development of additional fragmentation pathways associated with possible rearrangement of M^+. In this connection, the mass-spectral behavior of VII-X will be examined separately.

Peaks of $[M - H]^+$ ions (F_1) are observed in the mass spectra of I-VI in addition to molecular-ion peaks. The elimination of a hydrogen atom from M^+ can be assumed to take place from the 4 or 6 position. In these cases the process leads to the formation of a pseudoaromatic heteroring. Splitting out of hydrogen from the ortho position of the 2-aryl substituent with cyclization of the resulting radical center at the nitrogen atom of the heteroring, as observed in the mass-spectrometric fragmentation of phenylpyridines [2], dipyridyls [3], and 5-aryl-1,4-benzodiazepin-2-ones [4], seems no less likely. The C_2—N_3—C_4—C_5 fragment of the oxazinone heteroring coincides with the analogous fragment of benzodiazepin-2-ones, and, in analogy with them [4], the formation of $[M - 28]^+$ ions in the fragmentation of oxazinones can be linked with elimination of an H_2CN radical rather than a CO molecule. This conclusion is confirmed by the fact that an $[M - 28]^+$ ion peak is completely absent in the mass spectra of VII-X, in which the carbonyl group is retained, but the 4 position is substituted (Table 2).

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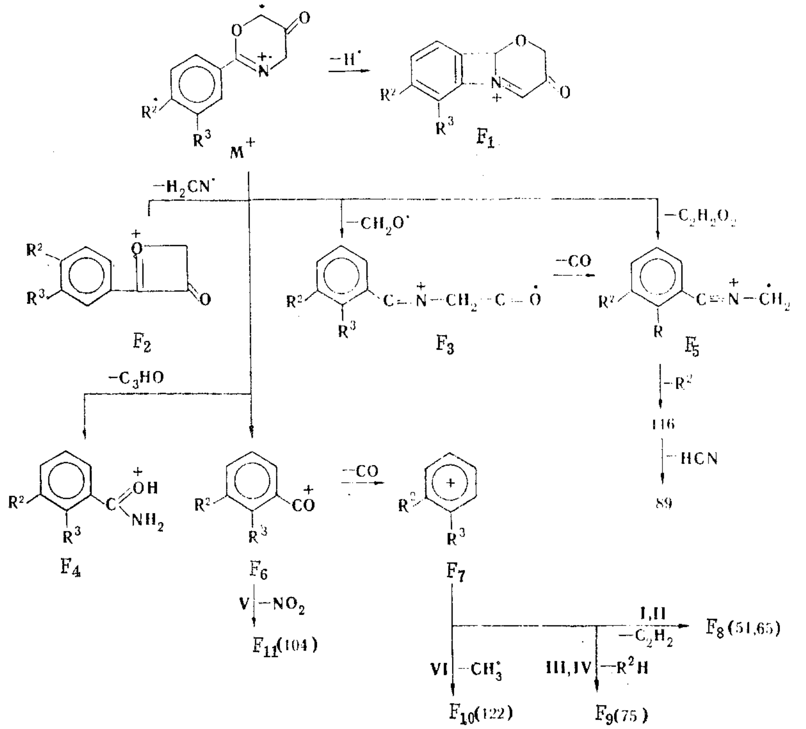
TABLE 1. Intensities of the Peaks of the Characteristic Fragment Ions in the Mass Spectra of I-VI (in percent of the total ion current)

Compound	Index of the M^+ ions									
	W_M	F_1	F_2	F_3	F_4	F_5	F_6	F_7	116	89
I	5,3	2,8	0,9	2,9	1,9	12,5	15,1	15,2	1,0	2,1
II	5,6	2,5	0,9	1,9	0,5	12,9	13,8	12,0	1,0	2,1
III	1,1	0,5	0,3	0,8	3,4	9,4	16,7	8,5	0,4	—
IV	4,0	1,6	0,6	2,2	1,6	10,0	14,3	4,7	1,5	2,3
V	1,0	0,3	0,3	1,4	5,9	3,1	4,2	—	2,4	2,0
VI	10,7	1,4	1,0	0,2	0,7	7,1	17,3	1,0	—	—

In contrast to 1,3-oxazin-6-ones, in the fragmentation of 1,3-oxazin-5-one does not observe a retrodiene reaction but rather successive elimination of H_2CO and CO molecules with the formation of F_3 and F_5 ions. The F_5 ions may also be formed in one step by elimination of a $C_2H_2O_2$ fragment from M^+. Such mass-spectral behavior of 1,3-oxazin-5-ones makes it possible to propose that the heteroring double bond in the M^+ ions of these compounds is not stabilized or that cleavage of the C_4–C_5 bond and subsequent fragmentation of the heteroring occur during ionization.



As a rule, the F_5 ion peaks have high intensities. Except for VI, their subsequent fragmentation involves the successive elimination of the R^2 substituent and an HCN molecule with the formation of common ions with m/e 116 and 89.* In the fragmentation of VI the F_5 ions split out a methyl radical.

In addition to the ions indicated above, F_4 ions (see the scheme presented above), which are formed as a result of the loss of the C_3HO group of atoms form M^+ and are probably the corresponding protonated (at the oxygen atom) amides, are common to the entire series of compounds.

The most intense peaks in the mass spectra of all of the investigated compounds are the peaks of benzoyl cations (F_6), the formation of which is possible from M^+, F_1, or F_2.

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

TABLE 2. Intensities of the Peaks of the Characteristic Fragment Ions in the Mass Spectra of VII-X (in percent of the total ion current)

Compound	Ions						
	M^+	$[M-RCN]^+$	$ArCO^+$	$ArCNH^+$	$ArCN^+$	$[M-C_7H_7]^+$	$C_7H_7^+$
VII	0,8	2,4	17,7	10,5	6,7	—	—
VIII	0,3	4,3	22,9	13,2	4,3	—	—
IX	0,2	3,2	19,2	10,6	4,3	3,6	9,6
X	0,7	1,8	14,7	3,2	2,3	14,2	9,1

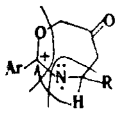
We investigated the dependence of the I_{F_6}/I_{M^+} value (where I_{F_6} and I_{M^+} are the intensities of the peaks of the corresponding ions) on the Hammett σ constant [5]. A linear correlation is observed for I, II, IV, and V. The dimethoxy compound deviates from this dependence, evidently because one cannot simply sum up the electronic effects of each substituent. It should be especially emphasized that the I_{F_6}/I_{M^+} value for III (R^2 = Cl) gives an anomaly (see Fig. 1). The physicochemical properties of this compound are also different from the properties of other oxazinones and will be discussed in a separate communication.

The observed linear dependence makes it possible to conclude that F_6 ions are formed only from M^+ in the fragmentation of I, II, IV, and V. In the case of III there are either several pathways for the formation of F_6 ions, or the M^+ ions undergo structural isomerization.

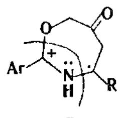
The F_6 benzoyl cations eliminate a CO molecule [6] (F_7 ions) and subsequently undergo fragmentation via various pathways, depending on substituent R^2.

Thus the fragmentation of I-VI under electron impact can be represented by a general scheme.

As we noted above, the mass-spectral behavior of 4-substituted oxazinones VII-X differs markedly from the fragmentation of I-VI. Peaks of F_2–F_5 ions that are common to the 4-unsubstituted compounds are completely absent in their spectra, and peaks of $[M-RCN]^+$ (R = H, CH_3, and C_6H_5, respectively, for VII, VIII and IX, X) and $[ArCNH]^+$ and $[ArCN]^+$ (Ar is a substituent in the 2 position) ions are observed. These data make it possible to conclude that during ionization the molecules of 4-substituted oxazinones undergo rearrangement (the structure of VII-X was proved by means of the high-resolution PMR spectra [1]) with expansion of the heteroring to a seven-membered ring due to the methylene group of substituent R^1, and their molecular ions may exist in two tautomeric forms (A and B):



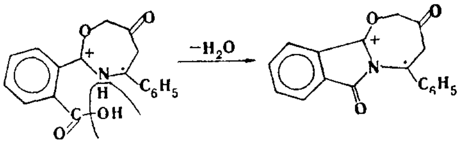
A



B

R = H, CH_3, C_6H_5

Form A determines the formation of $[M-RCN]^+$ and $ArCO^+$ ions, while form B determines the formation of $[ArCNH]^+$ and $[ArCN]^+$ ions. The existence of tautomeric form B, i.e., the presence of a hydrogen atom attached to the heteroring nitrogen atom, is confirmed indirectly by the mass spectrum of XI, in which an M^+ peak is not observed, but an $[M-H_2O]^+$ ion peak is present:



XI

Thus the introduction of even such an inert substituent as the methyl group in the 4 position sharply changes the mass-spectrometric properties of oxazinones. However, it should be noted that in the case of 4-benzyl-substituted compounds one observes, in addition to rearranged structures, M^+ ions with unchanged structures, as evidenced by the presence in their

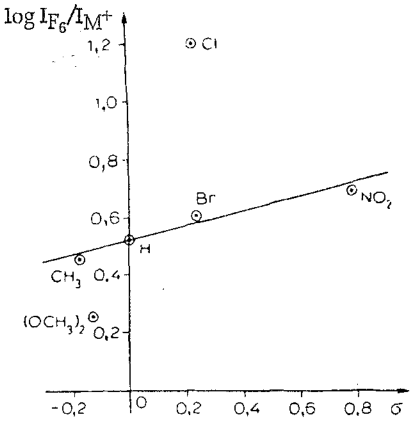


Fig. 1. Dependence of I_{F_6}/I_{M^+} on the Hammett σ substituent constants for I-VI. When the points for III and VI are excluded, correlation coefficient r = 0.988, and reaction constant ρ = 0.25.

TABLE 3. Mass Spectra of I-X

Compound	m/e values (relative intensities of the ion peaks in percent of the maximum peak)*
I	175 (31,7), 174 (16,6), 147 (6,0), 145 (19,3), 122 (12,8), 118 (8,4), 117 (82,6), 116 (6,5), 106 (11,1), 105 (99,5), 90 (17,0), 89 (14,0), 78 (8,7), 77 (100), 76 (13,2), 74 (6,4), 63 (10,0), 58 (15,7), 52 (7,9), 51 (58,8)
II	189 (36,0), 188 (15,6), 159 (13,7), 132 (10,6), 131 (9,4), 120 (12,0), 119 (100), 116 (7,2), 103 (8,6), 92 (7,3), 91 (87,3), 90 (10,5), 89 (15,1), 86 (10,1), 77 (14,8), 65 (77,8), 64 (14,2), 63 (18,1), 52 (10,9), 51 (22,6)
III	211 (2,2), 209 (6,6), 158 (18,1), 156 (56,6), 153 (6,7), 151 (20,1), 141 (32,7), 139 (100), 113 (15,0), 111 (52,8), 77 (8,1), 76 (15,4), 75 (58,8), 74 (24,8), 73 (9,8), 65 (7,7), 64 (7,6), 61 (8,2), 51 (19,1), 50 (6,3)
IV	255 (25,0), 253 (25,0), 225 (18,5), 223 (15,2), 197 (69,3), 195 (69,7), 185 (100), 183 (99,9), 157 (32,3), 155 (34,0), 116 (21,0), 98 (22,6), 97 (21,0), 89 (31,5), 86 (21,6), 76 (52,2), 75 (64,3), 74 (29,8), 58 (42,7), 51 (19,8)
V	220 (8,3), 190 (13,5), 167 (56,0), 162 (29,5), 150 (40,5), 121 (22,5), 116 (22,8), 109 (11,5), 104 (15,5), 89 (18,8), 81 (19,2), 77 (11,5), 76 (30,0), 75 (30,4), 74 (17,0), 69 (20,6), 65 (100), 63 (16,0), 53 (11,2), 51 (27,6)
VI	235 (54,1), 234 (7,2), 177 (40,8), 166 (9,3), 165 (100), 162 (21,7), 107 (7,3), 94 (8,4), 92 (8,3), 89 (10,7), 88 (15,8), 79 (25,6), 78 (8,5), 77 (20,8), 76 (7,7), 65 (12,0), 64 (8,9), 63 (12,7), 53 (8,0), 51 (21,4)
VII	189 (4,5), 188 (3,0), 162 (13,5), 161 (6,8), 146 (10,7), 145 (6,2), 131 (25,0), 130 (18,9), 117 (4,4), 105 (100), 104 (59,2), 103 (37,9), 91 (4,6), 77 (56,3), 76 (14,5), 75 (4,6), 74 (4,1), 63 (4,1), 52 (5,7), 51 (37,1)
VIII	203 (1,1), 162 (17,2), 146 (10,0), 145 (5,1), 130 (23,4), 122 (4,4), 118 (4,8), 117 (5,4), 106 (8,0), 105 (100), 104 (52,4), 103 (17,2), 91 (7,2), 78 (5,0), 77 (54,2), 76 (9,8), 75 (4,2), 63 (4,0), 57 (11,2), 51 (22,6)
IX	265 (3,0), 206 (6,0), 174 (19,1), 162 (16,2), 146 (19,1), 120 (7,9), 119 (6,9), 118 (14,8), 116 (6,8), 105 (100), 104 (55,6), 103 (21,9), 91 (49,9), 90 (7,0), 89 (7,9), 77 (57,1), 76 (8,9), 65 (12,2), 63 (8,0), 51 (33,8)
X	325 (5,0), 239 (96,9), 206 (15,8), 178 (13,6), 165 (100), 164 (20,8), 163 (15,0), 151 (25,1), 122 (14,8), 121 (14,0), 120 (14,0), 104 (20,8), 103 (20,4), 91 (63,5), 79 (30,6), 78 (20,9), 77 (46,2), 65 (28,9), 63 (17,0), 51 (30,9)

*The 20 most intense peaks are presented.

spectra of $[M - CH_2C_6H_5]^+$ and $[CH_2C_6H_5]^+$ ion peaks and low-intensity $[M - C_2H_2O_2]^+$ ion peaks (F_5).

EXPERIMENTAL

All of the investigated 2-aryl-5,6-dihydro-4H-1,3-oxazin-5-ones were obtained from 1-diazo-3-aroylaminopropan-2-ones by a single method.

A 3-mmole sample of the diazo ketone was dissolved in 30 ml of chloroform, and 0.6 g (6 mmole) of concentrated H_2SO_4 was added. The reaction mixture was then shaken vigorously, after which it was neutralized with sodium bicarbonate and treated with 10 ml of water. The chloroform layer was separated and dried over sodium sulfate. The solvent was removed, and the residue was washed with cold ether, dried, and recrystallized from ether.

The purity and individuality of the compounds were monitored by TLC and data from the IR, UV, and PMR spectra.

The mass spectra were obtained with a Varian MAT-44S spectrometer at an ionizing-electron energy of 70 eV, an emission current of 450 μA, and a temperature range of 80-170°C. A system for direct introduction into the ion source was used.

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THIAZOLIDINE-2,4-DIONE DERIVATIVES WITH AN SO GROUP OUTSIDE THE RING

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The condensation of the potassium salt of thiazolidine-2,4-dione with bis(β-chloroethyl)sulfide leads to bis[β-(thiazolidine-2,4-dion-3-yl)ethyl]sulfide, which is readily oxidized by H_2O_2 to bis[β-(thiazolidine-2,4-dion-3-yl)ethyl]sulfoxide. Products of condensation of the latter with oxo compounds were obtained. The structures of the synthesized compounds were proved by their UV and IR spectra.

It is known [1, 2] that 3-substituted thiazolidine-2,4-diones are oxidized by potassium permanganate in acetic acid to the corresponding thiazolidine-2,4-dione 1-sulfones. The formation of 1-sulfoxides is observed only in the 2-iminothiazolid-4-one series; the properties of 2-iminothiazolid-4-one 1-sulfoxides, particularly the UV spectra, have been studied in detail [3]. Thiazolidine derivatives that contain a sulfoxide (S=O) group outside the ring have not yet been described.

We have obtained bis[β-(thiazolidine-2,4-dion-3-yl)ethyl]sulfide (I) in 58% yield by condensation of the potassium salt of thiazolidine-2,4-dione with bis(β-chloroethyl)sulfide in dimethylformamide (DMF). Oxidation of the product with hydrogen peroxide in dioxane at 16°C leads to bis[β-(thiazolidine-2,4-dion-3-yl)ethyl]sulfoxide (II) in 60% yield.

Compounds I and II are colorless crystalline substances and are characterized by two absorption maxima, viz., a high-intensity maximum at 225 nm and a low-intensity maximum at 323.5 nm. The spectra of these compounds differ only slightly in intensity. However, oxidation of thiazolidines at the sulfur atom in the 1 position leads to the development of new absorption bands [3].

As in the case of unsubstituted thiazolidine-2,4-dione [4], the first band with an absorption maximum at 225 nm corresponds to p-π conjugation in the thiocarbonate chromophore, while the second band with an absorption maximum at 323.5 nm corresponds to an $n \to \pi^*$ transition of a carbonyl group (compare with the data for cyclopentanone [5]).

The IR spectrum of II is characterized by a high intensity S=O band at 1038 cm^{-1}, which corresponds to I.

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