THERMAL ISOMERIZATION OF THE ISOXAZOLE RING AND REARRANGEMENT PROCESSES IN THE MASS SPECTRA OF 3-ARYL-5-METHYLISOXAZOLE-4-CARBOXYLIC ACIDS

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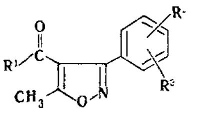
The mass spectra of 15 compounds of 3-aryl-5-methylisoxazole-4-carboxylic acid and their derivatives were investigated. Thermal isomerization of the isoxazole ring was observed for several derivatives of this series. The formation of rearranged pseudomolecular ions of the arylamines during the dissociative ionization of 3-aryl-5-methylisoxazole-4-carboxylic acids was examined on the basis of a study of the mass spectra of labeled compounds. It is assumed that there is a high probability of concerted elimination of several groups in the first step of the disintegration of the molecular ion.

We have previously examined [1] the mass spectrometry of some 3-aryl-5-methylisoxazole-4-carboxylic acids. The present paper is devoted to a study of the effect of structural factors on the character of the disintegration of the molecular ion in this series of compounds. The mass spectra of 15 compounds of 3-aryl-5-methylisoxazole-4-carboxylic acid and their derivatives (I-XV) were investigated. The mass spectra were obtained with a Varian MAT-CH-6 spectrometer at an ionizing-electron energy of 70 eV and an ionization-chamber temperature of 180°C.



I-XV

	R^1	R^2	R^3		R^1	R^2	R^3
I	OH	H	H	IX	NH_2	2-Cl	H
II	OH	3-NO_2	H	X	OCH_3	2-Cl	6-Cl
III	OH	3-NH_2	H	XI	OD	H	H
IV	OH	4-N=CHC_6H_4=2-OH	H	XII	OD	3-NO_2	H
V	OH	2-Cl	H	XIII	OD	3-ND_2	H
VI	OH	2-Cl	6-Cl	XIV	OD	2-Cl	H
VII	OC_2H_5	H	H	XV	OD	2-Cl	6-Cl
VIII	OCH_3	2-Cl	H				

The dissociative ionization of I-XV proceeds similarly in many respects. The principal paths of disintegration are associated with the formation of acetyl ions with mass 43 and ions with mass 143+m (R^2, R^3).* Peaks of $(M-CH_3)^+$ ions are also observed in all of the mass spectra, but their intensity is very low. An important peculiarity of the disintegration of the molecular ions of the acids is the formation of $(M-CO_2)^+$ ions.

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* The expression m(R^2, R^3) is the sum of the masses of the corresponding R^2 and R^3 radicals.

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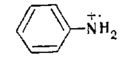
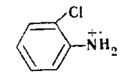
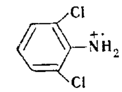
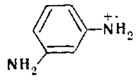
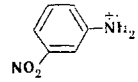
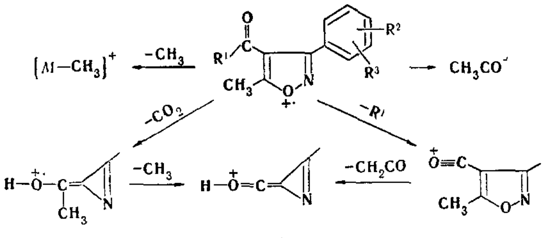
TABLE 1. Effect of Substitution in the Benzene Ring on the Relative Intensity of R^2, $R^3-C_6H_3-\overset{+\cdot}{N}H_2$ Ions

$R^2,R^3-C_6H_3-\overset{+\cdot}{N}H_2$	$I_i/\Sigma I_i\cdot 100\%$	$I_i/I_{43}\cdot 100\%$
	6,3	52,2
	4,2	43,2
	4,9	39,0
	1,5	23,4
	0,6	2,4

The elimination of CO_2 may proceed with both the participation of the oxygen atom of the carbonyl group through a six-membered transition state and with the participation of a nitrogen atom through a five-membered transition state. Ohashi and co-workers [2] have proposed a scheme including a six-membered transition state.

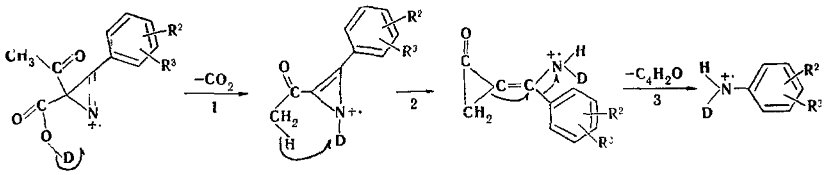


However, our investigation of the mass spectra of labeled compounds showed that the hydrogen atom can also migrate to the nitrogen atom.

This conclusion follows from the detection in the mass spectra of 3-aryl-5-methylisoxazole-4-carboxylic acids of peaks with mass 91 + m(R^2, R^3). Two structures – R^2, $R^3-C_6H_3-O^+$ and R^2, $R^3-C_6H_3-\overset{+\cdot}{N}H_2$ – are probable for these ions. An examination of the mass spectra of the deutero analogs of the acids shows that ions with mass 91 + m(R^2, R^3) in the mass spectra of the nondeuterated compounds fully contain the hydrogen of a carboxyl group. Thus, the structure of ions with mass 91 + m(R^2, R^3) should correspond to the structure of the pseudomolecular ions of aniline or the corresponding aromatic amines. It is interesting to note that the formation of R^2, $R^3-C_6H_3-\overset{+\cdot}{N}H_2$ ions should occur as a result of three successive migrations of two hydrogen atoms and of an aryl radical.

The formation of $R^2,R^3-C_6H_3-\overset{+\cdot}{N}H_2$ ions is not observed for the acid derivatives. The intensities of the peaks of the $R^2,R^3-C_6H_3-\overset{+\cdot}{N}H_2$ ions with respect to the total ion current and the intensities of the CH_3CO^+ ion peak are presented in Table 1. It follows from these data that substitution of the hydrogen atom in the ortho position of the benzene ring by a chlorine atom lowers the probability of migration as compared with a phenyl substituent only to a slight degree. The halogen atom in the transition state probably partially compensates for the negative –I effect through the +M effect. The formation of ions with mass 91 + m(R^2,R^3) in the mass spectrum of X shows that the C^1 atom of the benzene ring undergoes attack on the nitrogen atom side.

The $M-NO_2$ and $M-NH_2$ groups can only formally manifest a –I effect. As one should have expected, particularly pronounced inhibition of the reaction is observed when R = NO_2.



As shown by Nishiwaki [3, 4], isoxazole derivatives containing RO, RS, and NH_2 groups attached to the C^5 atom are capable of undergoing thermal valence isomerization to 1-azirine derivatives. In the recording of the mass spectra of methyl ester VIII and amide IX of 5-methyl-3-(2'-chlorophenyl)isoxazole-4-carboxylic acid with an MKh-1303 spectrometer at an input-system temperature of 250°, we observed a change in the intensities of the peaks with time; this indicated some sort of transformation of the substance introduced into the spectrometer.

A steady-state distribution of the intensities of the peaks, which corresponds to transformation product VIIIa or IXa, was established 40 min after introduction of the sample. The intensities of the peaks of some of the ions in the mass spectra of VIII, VIIIa, IX, and IXa are presented in Table 2. All of the values were taken in percent with respect to the intensity of the $(M-Cl)^+$ ion peak in the mass spectra of VIII or IX, respectively. It follows from an examination of the data in Table 2 that the $(M-Cl)^+$ ion peak is almost completely absent in the spectra of VIIIa and IXa, while the intensity of the molecular ion peak increases on the average by a factor of two. Consequently, the change in the mass spectra with time is due to isomer-

TABLE 2. Relative Intensities of the Peaks of Some Ions in the Mass Spectra of Methyl Ester VIII and Amide IX of 3-(2'-chlorophenyl)-5-methylisoxazole-4-carboxylic Acid and Their Isomerization Products (VIIIa and IXa)

Ions	Compound			
	VIII	VIIIa	IX	IXa
M^+	7,0	11,3	7,4	17,1
$(M-R^1)^+$	5,3	5,7	10,4	23,2
$(M-Cl)^+$	100,0	0	100,0	0
$(M-R^1-CH_2CO)^+$	27,0	3,6	19,7	4,0
CH_3CO^+	51,0	44,3	42,4	31,8

ization of starting materials VIII or IX, which leads to disruption of the aromatic structure of the isoxazole ring. The increase in the intensity of the molecular peak is a result of the absence of the disintegration $M^+ \rightarrow (M-Cl)^+$; this is due to the impossibility of the formation of the aromatic structure of the pyrylium cation.

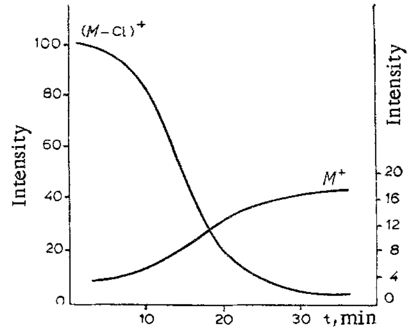
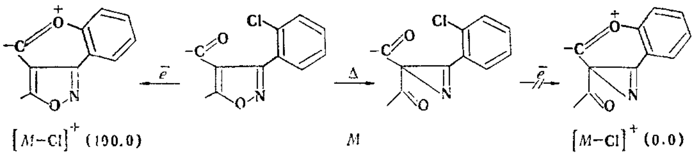


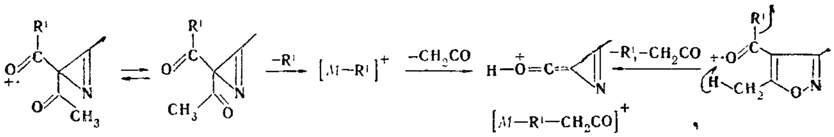
Fig. 1. Dependence of the intensity of the M^+ and $(M-Cl)^+$ ion peaks on time in the mass spectrum of 3-(2'-chlorophenyl)-5-methylisoxazole-4-carboxamide.



The time required for the conversion IX → IXa at an inlet temperature of 250° is 35-40 min (Fig. 1).

As seen from the data in Table 2, the absence of the process $M^+ \rightarrow (M-Cl)^+$, which is linked to the dissociation of a considerable fraction of the molecular ions, leads to an appreciable increase in the probability of disintegration via the path $M^+ \rightarrow (M-R^1)^+$. In addition, the probability of the process $M^+ \rightarrow (M-R^1-CH_2CO)^+$ decreases with unexpected sharpness. This fact can be explained by taking into account the possible transition states of the reaction to form the $(M-R^1-CH_2CO)^+$ ions for VIII, IX, and VIIIa, IXa.

In the case of isoxazole derivatives, the probability of concerted detachment of R^1 and CH_2CO is considerably higher than the probability of this process for the isomeric azirine owing to the quasiplanar configuration of the starting state. In other words, the concerted process



$M^+ \rightarrow (M-R^1-CH_2CO)^+$ should be characterized by a lower (in absolute value) value of the activation entropy ($\Delta S^{\neq} < 0$) for disintegration of the molecular ions of isoxazole derivatives. Thus, it can be assumed that the mechanism of concerted detachment of R^1 and CH_2CO groups plays a significant role in the formation of $(M-R^1-CH_2CO)$ ions.

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4. T. Nishiwaki, Chem. Commun., 945 (1970).