# REARRANGEMENT PROCESSES IN THE MASS SPECTRA OF SOME 3,5-DIMETHYLISOXAZOLE DERIVATIVES

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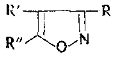
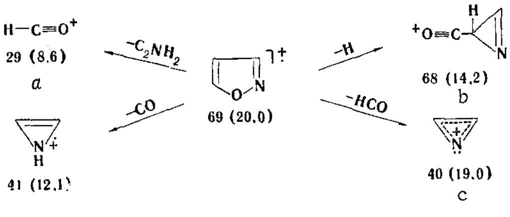
The mass spectra of isoxazole and some 3,5-dimethylisoxazole derivatives were investigated. Schemes for the formation of the principal rearranged ions are proposed on the basis of a study of the dissociative ionization of labeled compounds. Examples of the effect of electronic and steric factors on the probability of the existence of different channels for disintegration of the molecular ion are presented. It is shown that the formation of an ion with mass 82 during the dissociative ionization of a number of the investigated compounds occurs via different mechanisms as a function of the nature of the substituents in the 4 position of the isoxazole ring.

The opening of the isoxazole ring with subsequent formation of the isomeric molecular ion of a substituted 1-azirine is of great significance for the mass spectrometry of isoxazole and its derivatives. In this case, sterically favorable conditions develop for the occurrence of rearrangement processes. Interesting examples of the formation of rearranged ions can be observed in a number of 3,4,5-trisubstituted isoxazole derivatives. In the present paper we have investigated the mass spectra of isoxazole (I), 3,5-dimethyl-4-hydroxymethylisoxazole (II), (3,5-dimethyl-4-isoxazolyl)phenylcarbinol (III), (3,5-dimethyl-4-isoxazolyl)diphenylcarbinol (IV), 3,5-dimethylisoxazole-4-carboxylic acid (V), and the deuterated derivatives of II-V (VI-IX).



|  | R | R' | R'' | $W_M$ | $S_1/_2$ |
|---|---|---|---|---|---|
| I | H | H | H | 21.0 | 3 |
| II | $CH_3$ | $CH_2OH$ | $CH_3$ | 7.6 | 6 |
| III | $CH_3$ | $(C_6H_5)_2COH$ | $CH_3$ | 6.8 | 12 |
| IV | $CH_3$ | $(C_6H_5)_2COH$ | $CH_3$ | 1.8 | 12 |
| V | $CH_3$ | COOH | $CH_3$ | 3.8 | 9 |
| VI | $CH_3$ | $CH_2OD$ | $CH_3$ |  |  |
| VII | $CH_3$ | $C_6H_5CHOD$ | $CH_3$ |  |  |
| VIII | $CH_3$ | $(C_6H_5)_2COD$ | $CH_3$ |  |  |
| IX | $CH_3$ | COOD | $CH_3$ |  |  |

The most typical ions that characterize the dissociative ionization of isoxazole and its 3,5-disubstituted derivatives are associated with the formation of structural fragments *a*, b, and c. Depending on the substituents in the 3 and 5 positions of the ring, competition in the formation of the indicated types of ions is observed.



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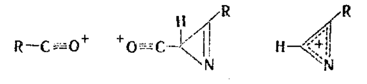
The relative distribution of ions *a*, b, and c, as well as $M^+$, in the mass spectra of isoxazole, 3,5-dimethylisoxazole, and 3,5-diphenylisoxazole [1] are presented below.



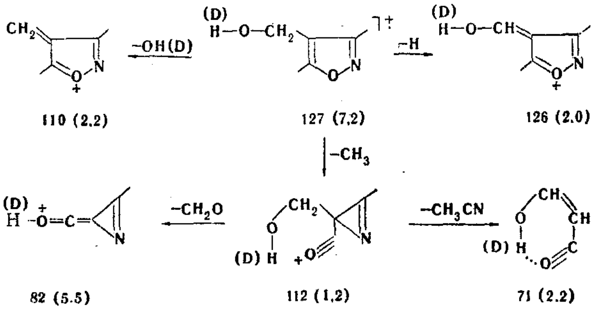
| | *a* | b | c | *M*+ |
|---|---|---|---|---|
| $R=H$ | 0.41 | 0.68 | 0.91 | 1.00 |
| $R=CH_3$ | 0.72 | 1.00 | 0.71 | 0.80 |
| $R=C_6H_5$ | 1.0 | 0.14 | 0.07 | 0.60 |

It follows from the data presented above that ions b and c, the peaks of which are intense in the mass spectra of isoxazole and 3,5-dimethylisoxazole, lose their significance appreciably in the case of the dissociative ionization of 3,5-diphenylisoxazole. The strongest interaction of charge with substituent R, which leads to considerable stabilization of the structure, is observed for $R-C\equiv O^+$ ions. While the probability of the formation of $RCO^+$ ions increases in the order $R=H<CH_3<C_6H_5$, the relative intensities of the peaks of the molecular ions decrease in the same order. We have also noted the existence of an inverse dependence between the intensities of the $M^+$ and $RCO^+$ ion peaks for other isoxazole derivatives [2].

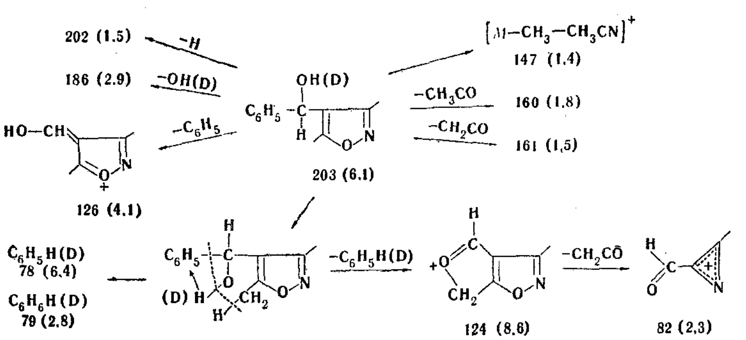
Despite the intense molecular-ion peak in the mass spectrum of isoxazole, its resistance to electron impact is appreciably lower than that of other five-membered aromatic heterocycles. Thus, the following $W_M$ values are observed for pyrazole, thiophene, furan, imidazole, pyrrole, and isoxazole: 45.9, 30.6, 27.4, 27.1, 26.0, and 21.0.

Many of the fragment ions in the mass spectra of II-IX are rearranged ions, the formation of which usually proceeds through six-membered or five-membered transition states. The dissociative ionization of 3,5-dimethyl-4-hydroxymethylisoxazole was examined in [3]. An investigation of the mass spectrum of deuterated derivative VI made it possible to accurately determine the probable paths for the formation of several ions (for example, ions with mass 71).

The dissociative ionization of III is distinguished by a considerable number of competitive directions of disintegration; this is reflected in the high (12) $S_{1/2}$ value (low disintegration selectivity [4]).



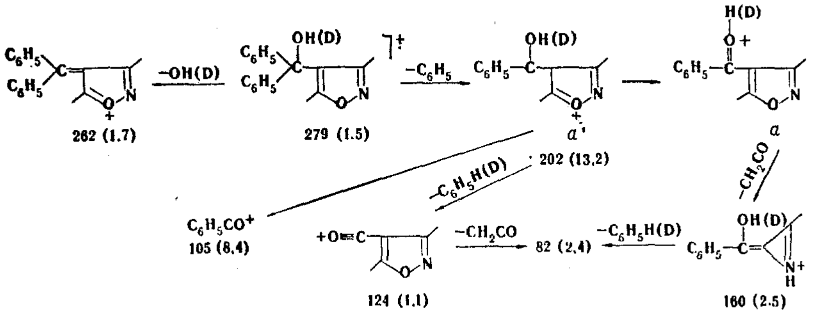
The stripping of H, OH, and $C_6H_5$ particles from the molecular ion leads to the formation of one of three possible conjugated structures (for example, the structure of an ion with mass 126).



The maximum peak in the mass spectrum of III corresponds to the $(M-C_6H_7)^+$ ion with mass 124. In contrast to the $(M-C_6H_5)^+$ ion peak with mass 126, no isotopic shift in the mass spectrum of deuterated derivative VII is observed for the peak of this ion. The formation of an $(M-C_6H_7)^+$ ion is a relatively low-energy process. The relative intensities ($I_i/I_{124}$) decrease appreciably for all ions [except for $M^+$ and $(M-CH_2CO)^+$ ions] on passing from ionizing electron energies of 50 eV to 15 eV. Furthermore, the mass spectrum of III contains intense $C_6H_6{}^+$ and $C_6H_7{}^+$ ion peaks, the majority of which, as demonstrated by the mass spectrum of VII, contain hydroxyl-group hydrogen. It follows from these data that the formation of ions with mass 124 occurs directly from $M^+$ and is associated with the migration of one or two hydrogen atoms to the benzene ring and splitting out of $C_6H_7$ or $C_6H_6$ and H particles. When the charge is localized on the benzene ring during disintegration of the rearranged $M^+$ ion, $C_6H_7{}^+$ or $C_6H_6{}^+$ ions are formed.

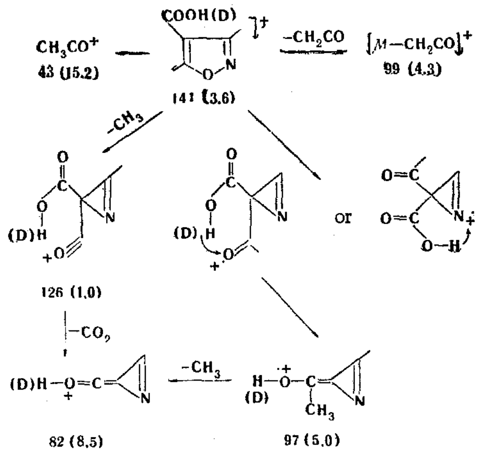
When the hydrogen atoms in the hydroxymethyl group are substituted successively [II ($CH_2OH$) → III ($C_6H_5CHOH$) → IV [($(C_6H_5)_2OH$)]], one observes an appreciable decrease in the resistance of the molecule to electron impact, and the $W_M$ value decreases most markedly when a second phenyl substituent is introduced. An analysis of Stuart–Briegleb models demonstrates that the rotational mobility of the benzene rings in the IV molecule is markedly hampered because of steric hindrance to rotation created by the methyl groups; this should apparently lower the stability of the molecular ion.

The impossibility of coplanar orientation of the benzene rings in the structure of the $(M-OH)^+$ ion with mass 262 causes a considerable predominance of detachment of a phenyl radical rather than a hydroxyl radical. As seen from the disintegration scheme, the maximum peak in the mass spectrum of IV corresponds to the $(M-C_6H_5)^+$ ion.



On examining the dissociative ionization of IV, one's attention is directed to the absence of an expressed tendency for the formation of $(C_6H_5)_2C=\overset{+}{O}-H$ ions. A possible reason for the preferred formation of $HetC_6H_5C=\overset{+}{O}-H$ ions [$(M-C_6H_5)^+$] (Het = hetaryl) as compared with $(C_6H_5)_2C=\overset{+}{O}-H$ ions may be the considerable stabilization of the former due to *a* → *a'* resonance.

Some regularities in the dissociative ionization of isoxazole-4-carboxylic acids were examined in [2]. The most important direction for the disintegration of the molecular ion of the latter is elimination of $CO_2$, which is directly associated with isomerization of the isoxazole ring during electron impact. The formation of $(M-CO_2)^+$ ions can apparently proceed through both a six-membered transition state with participation of an oxygen atom and through a five-membered transition state with participation of a nitrogen atom.



Relatively intense peaks of ions with mass 82 are present in the mass spectra of 3,5-dimethylisoxazoles II-V. An examination of the mass spectra of the deuterated compounds indicates that, in the case of II and V, these ions contain hydroxyl-group hydrogen (the corresponding isotopic shift is observed). In addition, most of the ions with mass 82 in the mass spectra of III and, particularly, IV do not contain hydroxyl hydrogen (an isotopic shift is not observed).

It follows from these data that the formation of the ions under consideration can occur by different paths. The reaction $M^+ \rightarrow (M-RR'CO)^+ \rightarrow (M-RR'CO-CH_3)^+$, which is responsible for the appearance of ion peaks with mass 82 in the mass spectrum of II, loses its significance in the case of the dissociative ionization of III and, particularly, IV. The retardation of the elimination of an RR'CO particle by the molecular ion when hydrogen atoms in the $CH_2OH$ group are replaced by bulky phenyl groups is probably associated with steric hindrance to the formation of the cyclic transition state of this reaction.

## EXPERIMENTAL

The mass spectra of I-IX were obtained with an MKh-1303 mass spectrometer at an ionizing electron energy of 50 eV and an ionization-chamber and inlet-system temperature of 200-250°. Peaks with intensities above 5% of the maximum are presented.

### Mass Spectra of Compounds I-IX

I: 26 (12,7), 27 (11,8), 29 (43,2), 30 (6,9), 37 (9,0), 38 (21,8), 39 (25,1), 40 (95,0), 41 (60,5), 42 (16,9), 68 (71,3), 69 (100,0), 70 (5,4).

II: 27 (13,0), 29 (8,8), 31 (8,6), 39 (17,1), 40 (9,1), 41 (13,4), 42 (34,2), 43 (100,0), 52 (6,6), 53 (6,1), 54 (7,6), 55 (6,8), 56 (9,4), 57 (8,5), 66 (10,5), 67 (9,6), 68 (9,9), 70 (7,5), 71 (10,8), 82 (27,4), 84 (26,8), 109 (15,6), 110 (10,9), 112 (5,8), 126 (9,8), 127 (36,0).

III: 27 (5,9), 39 (12,0), 40 (8,2), 41 (10,6), 42 (12,2), 43 (63,0), 51 (21,0), 56 (8,2), 65 (8,3), 69 (13,0), 76 (6,5), 77 (53,0), 78 (75,0), 79 (32,6), 80 (7,9), 82 (26,6), 84 (41,0), 91 (17,1), 102 (13,1), 103 (14,8), 105 (34,4), 108 (21,8), 115 (15,6), 124 (100,0), 125 (13,1), 126 (47,3), 129 (8,4), 131 (9,4), 144 (30,4), 145 (12,9), 147 (16,1), 160 (20,4), 161 (16,9), 170 (7,3), 186 (34,0), 187 (10,1), 202 (17,5), 203 (70,5), 204 (10,5).

IV: 39 (10,5), 40 (9,9), 41 (12,0), 42 (36,6), 51 (17,6), 76 (5,6), 77 (51,7), 78 (10,5), 82 (18,3), 91 (6,3), 105 (63,4), 124 (8,4), 145 (6,3), 151 (6,3), 152 (7,0), 155 (10,5), 160 (19,0), 165 (9,1), 176 (10,5), 177 (7,0), 178 (9,1), 182 (8,4), 201 (10,5), 202 (100,0), 203 (14,8), 217 (7,7), 218 (14,8), 246 (26,7), 261 (12,0), 262 (11,3), 279 (11,3).

V: 27 (31,4), 29 (14,0), 30 (9,0), 38 (11,5), 39 (31,4), 40 (21,0), 41 (35,0), 42 (50,0), 43 (100,0), 45 (8,5), 51 (7,6), 52 (10,2), 53 (7,6), 54 (41,5), 55 (21,0), 68 (8,5), 81 (8,5), 82 (56,0), 84 (55,0), 97 (33,0), 99 (28,4), 126 (6,8), 141 (24,0).

VI: 39 (18,2), 40 (9,1), 41 (13,1), 42 (30,2), 43 (100,0), 53 (7,1), 54 (6,2), 55 (7,3), 57 (6,2), 68 (13,2), 72 (12,6), 83 (27,1), 85 (29,6), 109 (15,6), 110 (11,2), 113 (7,3), 127 (16,3), 128 (40,5).

VII: 39 (16,0), 41 (11,8), 42 (18,6), 43 (96,0), 55 (6,4), 56 (8,1), 64 (7,9), 69 (16,3), 77 (26,1), 78 (43,0), 79 (56,2), 80 (34,3), 82 (16,3), 83 (10,6), 84 (9,7), 85 (9,7), 91 (13,4), 92 (16,5), 102 (12,9), 105 (30,6), 108 (23,2), 115 (12,3), 116 (7,9), 124 (100,0), 125 (12,1), 127 (60,2), 128 (8,3), 142 (10,6), 144 (29,2), 146 (7,2), 148 (18,2), 161 (23,8), 162 (17,3), 170 (10,3), 203 (23,8), 204 (76,3), 205 (12,1).

VIII: 39 (16,2), 41 (12,0), 42 (7,1), 43 (39,2), 51 (18,2), 77 (60,2), 78 (10,2), 82 (19,6), 91 (6,1), 105 (70,4), 124 (9,3), 146 (7,2), 151 (7,2), 156 (10,3), 161 (20,2), 176 (12,1), 177 (7,0), 202 (14,1), 203 (100,0), 204 (13,9), 217 (7,3), 218 (13,6), 246 (23,8), 247 (6,2), 260 (10,1), 261 (7,9), 262 (11,3), 280 (12,1).

IX: 38 (6,3), 39 (41,2), 40 (21,6), 41 (39,1), 42 (43,6), 43 (100,0), 51 (7,3), 52 (11,2), 53 (6,8), 54 (12,1), 55 (30,4), 68 (13,5), 81 (8,8), 82 (12.8), 83 (58,0), 85 (16,3), 86 (16,7), 98 (24,3), 100 (17,2), 142 (25,3).

## LITERATURE CITED

1. R. A. Khmel'nitskii, K. K. Zhigulev, S. D. Sokolov, and L. P. Tsurkanova, Zh. Organ. Khim., 6, 2162 (1970).
2. K. K. Zhigulev, R. A. Khmel'nitskii, M. A. Panina, I. I. Grandberg, and B. M. Zolotarev, Khim. Geterotsikl. Soedin., 889 (1972).
3. M. Ohashi, H. Kamachi, H. Kakisawa, A. Tatematsu, H. Yoshirimi, H. Kano, and H. Nakata, Org. Mass Spectrom., 2, 195 (1969).
4. R. A. Khmel'nitskii, K. K. Zhigulev, and S. D. Sokolov, Izv. Sel'skokhoz. Akad. im. Timiryazeva, 1, 197 (1971).