MASS SPECTRA OF IMIDAZO[2,1-b]THIAZOLE AND THIAZOLO[3,2-*f*]XANTHENE DERIVATIVES

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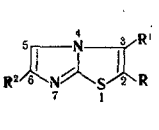
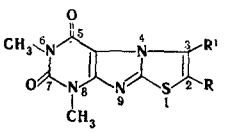
The general principles of the mass-spectrometric disintegration of imidazo[2,1-b]thiazole and thiazolo[3,2-*f*]xanthene derivatives were established, and the characteristic fragments were identified. Disintegration proceeding with cleavage of the bonds in the thiazole ring of the 2(3)-ring system is characteristic of all of the investigated compounds. The cleavage of the S–C bonds, which are the weakest in the investigated systems, proceeds especially readily. Intense peaks of ions due to stepwise disintegration of the pyrimidine ring are also observed in the spectra of thiazoloxanthenes.

Up until now inadequate study has been devoted to the fragmentation of condensed heteroaromatic systems during dissociative ionization. In particular, of the class of imidazothiazoles, an interesting peculiarity of which is the presence of a bridging nitrogen atom in the molecule, only some derivatives of 6-phenylimidazo[2,1-b]thiazole and thiazole[3,2-a]benzimidazole [1, 2] have been investigated.

We have investigated the disintegration of imidazo[2,1-b]thiazole (I) and its various substituted derivatives (II-V) and of thiazolo[3,2-*f*]xanthene derivatives (VI-IX) under electron impact. The synthesis of I-V and VI-IX was previously described in [3-6].



I-V



VI-IX

I R=R¹=R²=H; II R=CH_3, R¹=R²=H; III R=$COCH_3$, R¹=CH_3, R²=H; IV R=R¹=H, R²=COOH; V R=R¹=H, R²=$COOCH_3$; VI R=R¹=H; VII R=CH_3, R¹=H; VIII R=H, R¹=CH_3; IX R=R¹=CH_3

The mass spectra of I-IX are presented in Table 1.

The molecular ion of imidazothiazole I is characterized by high stability with respect to electron impact (W_M=41.8) and practically only the molecular ion peak is present in the spectrum of I at an ionizing electron energy of 12 eV. Peaks of both nitrogen-containing and sulfur-containing fragments formed during cleavage of various bonds in the imidazole and thiazole rings of the two-ring system appear at 50 eV.

The principal paths of disintegration of imidazothiazole I are presented in the scheme below. The ejection of an SH· group from the molecular ion of imidazothiazole I is not observed in the spectrum. This confirmed our previously expressed assumption [2] regarding the participation of hydrogen atoms from the alkyl group in the 2 or 3 position of the two-ring system in the splitting out of an SH group. One might have assumed several different structures for each of the ions with mass numbers m/e 84, 72, 71. However, a comparison of the spectra of imidazothiazole I and derivatives II and III showed that the mass numbers of the indicated ions do not shift on introduction of substituents into the thiazole ring. This fact provides a

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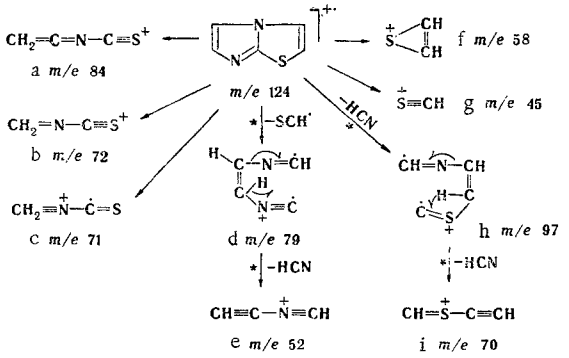
TABLE 1. Mass Spectra of Imidazo[2,1-b]thiazole and Thiazolo[3,2-*f*]-xanthene Derivatives

Compound	Mass spectra
I	39 (3,6), 40(3,5), 41 (1,6), 44 (3,5), 45 (8,5), 46 (5,6), 52 (12,7), 53 (3,1), 57 (6,4), 58 (12,7), 59 (2,4), 62 (1,1), 69 (2,4), 70 (14,5), 71 (9,3), 72 (4,5), 79 (14,5), 80 (2,2), 84 (5,6), 97 (7,3), 98 (1,8), 124 (100), 125 (7,3), 126 (4,7). W_m=41,8%
II	39 (16,7), 40 (5,3), 41 (3,1), 42 (1,4), 43 (1,4), 44 (11,4), 45 (7,2), 46 (1,4), 50 (2,6), 51 (3,8), 52 (11,1), 53 (9,4), 54 (3,3), 56 (2), 57 (8,3), 58 (7,5), 59 (2), 60 (5,3), 66 (2,8), 67 (3,1), 69 (5,8), 70 (5,6), 71 (9,9), 72 (7,2), 78 (2), 79 (6,4), 80 (18,1), 81 (2,1), 83 (4,5), 84 (11,1), 85 (2,2), 93 (3,9), 94 (2,2), 105 (2,6), 110 (7,5), 111 (3,8), 137 (27,8), 138 (100), 139 (9,7), 140 (5). W_m=27,6%
III	39 (16,7), 40 (6,4), 41 (3,5), 42 (19,4), 43 (41,7), 44 (3,9), 45 (9,4), 51 (4,2), 52 (9,7), 53 (3,9), 57 (7,2), 58 (4,4), 59 (8,1), 66 (6,1), 68 (2,5), 69 (6,9), 70 (7,5), 71 (8,1), 72 (4,7), 80 (3,2), 83 (3,9), 84 (8,3), 93 (25), 94 (8,3), 96 (3,3), 105 (2,6), 110 (3,9), 111 (3,2), 137 (22,2), 138 (13,6), 151 (2,8), 165 (91,7), 166 (9,4), 167 (5,3), 180 (100), 181 (2,5), 182 (6,3). W_m=20,5%
IV	39 (3,8), 40 (5,4), 41 (2), 44 (13,7), 45 (28), 46 (8,2), 51 (5), 52 (13,5), 53 (7,4), 57 (9,3), 58 (38,2), 59 (6), 60 (2,8), 64 (2), 69 (4,3), 70 (17,6), 71 (7,7), 72 (8,1), 79 (20,6), 83 (4), 84 (4), 85 (2), 96 (2,8), 97 (5,5), 123 (9,6), 124 (44), 125 (3,8), 126 (2,4), 151 (33,8), 152 (2,9), 153 (2), 168 (100), 169 (8,5), 170 (5,4). W_m=21,15%
V	39 (2,6), 40 (2,7), 43 (2), 44 (7,9), 45 (14,4), 46 (2,6), 51 (3,5), 52 (7,9), 53 (5,7), 57 (4,8), 58 (29,4), 59 (6,1), 69 (2,5), 70 (11,1), 71 (3,5), 72 (3,2), 79 (23,5), 83 (4,4), 84 (2), 97 (2,7), 98 (3,8), 122 (14,4), 123 (75), 124 (6,4), 125 (4,1), 152 (100), 153 (12), 154 (5,5), 182 (70,5), 183 (7), 184 (3,8). W_m=21,2%
VI	40 (3), 41 (3,8), 42 (5,2), 44 (2,7), 45 (4,8), 52 (4,0), 53 (2), 54 (2), 56 (4,1), 57 (5,8), 58 (15,8), 59 (2,2), 66 (2,3), 67 (9,1), 70 (6,7), 72 (2,9), 77 (2), 79 (2,1), 80 (3,0), 81 (2,3), 84 (3,4), 98 (2,1), 99 (8,5), 100 (2,1), 110 (10,3), 111 (2,6), 118 (2,4), 124 (12,6), 125 (8,2), 126 (2,6), 136 (2,0), 150 (12,6), 151 (47), 152 (15,9), 153 (3,8), 178 (7,2), 179 (18,2), 180 (3,5), 207 (4,8), 236 (100), 237 (13,2), 238 (6,5). W_m=24,3%
VII	39 (13,7), 40 (3,5), 41 (4,8), 42 (10), 43 (3,4), 44 (4,9), 45 (7,8), 52 (2,8), 53 (3,1), 54 (3,0), 55 (2,2), 56 (3,7), 57 (2,1), 58 (2,4), 66 (3,0), 67 (11,9), 68 (2,4), 69 (2,2), 70 (7,45), 71 (10,4), 79 (2,2), 80 (4,4), 81 (3,3), 82 (6,7), 83 (2,4), 93 (3,4), 94 (3,9), 96 (2,0), 97 (3,1), 98 (4,8), 99 (9,8), 124 (4,9), 125 (7,2), 126 (2,8), 138 (12,2), 139 (9,2), 163 (2,4), 164 (22,7), 165 (44,4), 166 (9,6), 167 (3,3), 192 (7,7), 193 (24,4), 194 (4,4), 221 (5,6), 250 (100), 251 (13,2), 252 (5,8). W_m=21,3%
VIII	39 (12,4), 40 (3,2), 41 (3,5), 42 (7,4), 44 (2,8), 45 (3,1), 53 (2,1), 54 (2,1), 56 (4,1), 58 (2,6), 59 (7,4), 66 (4,1), 67 (7,95), 70 (6,8), 71 (5,4), 72 (12,4), 80 (2,7), 81 (2,1), 98 (2,4), 99 (13,5), 122 (5,6), 123 (2,6), 124 (6,7), 125 (6,3), 126 (3,0), 138 (10,2), 139 (8,0), 163 (3,0), 164 (13,7), 165 (44,5), 166 (13,7), 167 (3,3), 192 (7,0), 193 (19,1), 194 (3,5), 221 (4,1), 250 (100), 251 (14,3), 252 (6,7). W_m=21,3%
IX	39 (3,2), 41 (3,2), 42 (7,6), 44 (2), 45 (2,8), 51 (2), 52 (3), 53 (17,2), 54 (3,2), 56 (2,4), 58 (2,4), 59 (6,8), 67 (8,4), 68 (2), 70 (4), 71 (3,6), 72 (3,6), 80 (3,2), 85 (3,6), 86 (3,6), 93 (2,4), 99 (13,2), 111 (2), 126 (2,0), 137 (2,4), 138 (3,2), 139 (2), 151 (2), 152 (9,2), 153 (9,6), 154 (2,6), 178 (22), 179 (32), 180 (7,6), 181 (2,4), 206 (7,6), 207 (19,6), 208 (4), 235 (5), 264 (100), 265 (6,4). W_m=24,4%

basis for assuming that the formation of ions with m/e 84, 72, and 71 occurs exclusively during the cleavage of the SC bond in the S_1-C_2 position.



The other possible paths of the formation of these ions, for example, by cleavage of C_2-C_3 or C_3-C_4 bonds, apparently are not realized. All of the information set forth above enabled us to assign structures a, b, and c to the fragments under consideration.

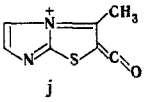
On the basis of the intensity ratio of the peaks of the fragments, elimination of SCH· from the molecular ion to give d and formation of the $+S\langle^{CH}_{CH}\|$ ion (f) should be considered to be the most favorable

disintegrative processes. These ions, and the $+S \equiv CH$ ion (g) also observed in the spectrum, were characteristic for all of the imidazothiazole derivatives that we previously investigated [2].

Thus, as seen from the scheme presented above, the molecular ion of imidazothiazole I disintegrates due to cleavage of two or three bonds, one of which in most cases is the S–C (1-2 or 1-8) bond. One should note the successive elimination of two HCN molecules leading to the appearance in the spectrum of ions h and i as the only exception to this. The data obtained attest to the preferableness of cleavage of the S–C bond during the disintegration of the molecular ion of imidazothiazole.

An examination of the mass spectrum of 2-methylimidazothiazole II showed that the introduction of a methyl group leads to a substantial decrease in the stability of the molecular ion (see (Table 1). An intense $(M-H\cdot)^+$ peak appears in the spectrum of II; this is explained by the ease of stabilization of the radical center in the ion formed in this case [2]. The disintegration of 2-methylimidazothiazole is basically similar to the disintegration of imidazothiazole I. The only difference is the fact that HCN in II is eliminated from the $(M-H\cdot)^+$ ion rather than from the molecular ion. As expected, the peak of the $(M-SH_3\cdot)^+$ ion is observed in the spectrum of II, and the mass numbers of ions f, g, h, and i increase by 14 units. The mass numbers of ions a, b, and c remain unchanged; this is in agreement with the structures proposed for them.

The stability of the molecular ions of 2-acetyl-3-methylimidazothiazole (III) with respect to electron impact falls to 20.5% as a consequence of the advantageousness of detachment of an acetyl group. The intense (42%) peak of the $C\overset{+}{O}CH_3$ ion is observed in the spectrum of imidazothiazole III, and the most intense peak (92%) after the molecular ion peak belongs to the $(M-CH_3\cdot)^+$ fragment. This is explained by the high stability of ion j, which is formed during the elimination of a CH_3 group.



j

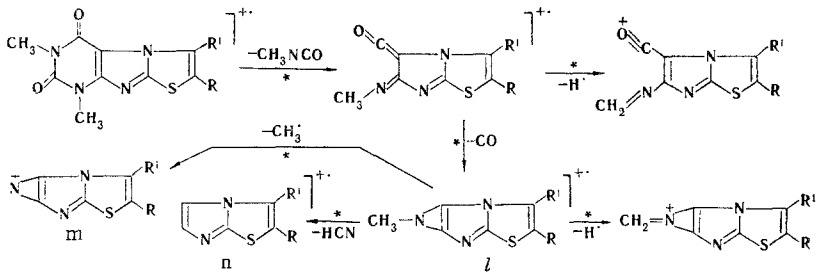
The ejection of ketene from the molecular ion of III, as in the case of acetyl derivatives of thiazolobenzimidazoles and 6-phenylimidazothiazole [2], is less advantageous. The successive ejection of CO, CS, and HCN groups occurs during the subsequent disintegration of the $(M-CH_3\cdot)^+$ ion. This fragmentation path is the dominant one. Peaks of the a, b, c ions that are typical for imidazothiazole compounds are also observed in the spectrum of III.

The stability of the molecular ions with respect to electron impact for carboxy and carbomethoxy derivatives IV and V is ~21%. The first act in the fragmentation of these compounds is elimination of OH· (IV) and $OCH_3\cdot$ (V) groups. The high intensity of the peak of the ion with m/e 151 that is formed in this case is explained by the ease of stabilization of the radical center in it. During the next act in the disintegration of this ion, a CO molecule is ejected to give an ion with m/e 123. This fragmentation path is the primary path in the spectrum of V, and ions with m/e 151 and 123 have relative intensities of 100 and 76.5%, respectively. The further disintegration of the ion with m/e 123 proceeds with successive ejection of CS and HCN particles, as evidenced by the corresponding metastable transitions. Peaks of ions d and e that are typical for imidazole[2,1-b]thiazole derivatives are therefore observed in the spectrum. In addition, the spectrum of V contains peaks of ions with m/e 58 and 45 (f and g) that are peculiar to imidazothiazoles that do not have substituents in the thiazole ring.

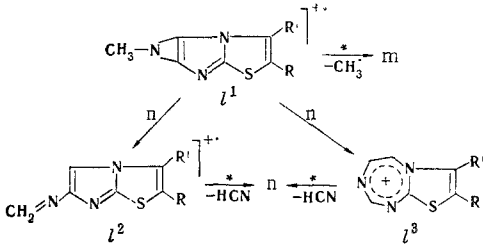
The more advantageous process in the spectrum of acid IV is decarboxylation of the molecular ion. The subsequent disintegration of the resulting ion with m/e 124 is similar to the fragmentation of the molecular ion of imidazothiazole I. The only substantial difference in the spectra of I and IV below m/e 124 proves to be the relatively higher intensity of the peaks of ions f and g. This is apparently explained by the fact that the ions of the indicated structures are formed not only during disintegration of the $(M-CO_2)^{+\cdot}$ ion but also directly from the molecular ion.

Thus disintegration with cleavage of the bonds in the thiazole ring, mainly with cleavage of the S–C bonds, is characteristic for all of the investigated imidazo[2,1-b]thiazole derivatives.

At present, the mass spectra of various xanthenes have been examined in detail [7], but there are no data available in the literature for thiazoloxanthenes. An analysis of the mass spectra obtained in this showed that the disintegration of thiazolo[3,2-*f*]xanthenes (VI-IX) can be described by a general scheme and that the principal direction of fragmentation is stepwise disintegration of the pyrimidine ring of the three-ring system, which is represented below:



According to the values of the metastable peaks, ion M in the spectra of all of the investigated thiazoloxanthenes may disintegrate with ejection of both a CH_3 group and an HCN group to give ions m and n, respectively. The elimination of a methyl group is easily accepted if it is assumed that ion *l* has the structure presented in this scheme. At the same time, splitting out of an HCN group from the ion of this structure is unlikely. The observed increase in the mass number of ion n by 14 units in the spectra of 2- and 3-methyl derivatives VII and VIII and by 28 units in the spectrum of 2,3-dimethyl derivative IX as compared with the thiazole-ring-unsubstituted thiazoloxanthene VI proves that splitting out of HCN does not involve the thiazole portion of the molecule. It is therefore logical to assume that ion M may exist in the form of different structures, for example, l^1, l^2, and l^3, which are presented below.



Elimination of an HCN group from ions with structures l^2 and l^3 will lead to fragment n. Similar fragmentation was previously described for 3-methylxanthene. In addition to the fragments presented in scheme 2, peaks of ions f and g that are typical for the imidazo[2,1-b]thiazole system are observed in the spectra of VI-IX. The spectra of thiazoloxanthenes that have methyl substituents in the thiazole ring (VII-IX) contain the peak of the $\overset{+}{C}H_2-C\equiv CR$ ion that is characteristic for alkyl derivatives of imidazothiazole [2]. The existence of the ions listed above provides evidence that, despite the peculiarities introduced into the disintegration of molecules VI-IX by the presence of a dimethylhydroxypyrimidine ring, the fragmentation directions that are common to imidazothiazoles are also peculiar to these compounds.

Thus a comparison of all of the spectra that we investigated shows that disintegration with cleavage of the bonds in the thiazole ring of the two(three)-ring system is characteristic for imidazo[2,1-b]thiazole and thiazole[3,2-*f*]xanthene derivatives. Similar data were previously obtained for substituted thiazole-[3,2-a]benzimidazoles [2]. As a rule, one of the S–bonds, which can apparently be considered to be the weakest in the heterocycles under examination, is cleaved. These data are in agreement with the chemical properties of the investigated compounds [5, 8, 9]. The introduction of a dimethyldihydroxypyrimidine ring into the molecule leads to the appearance of fragments due to the characteristic stepwise disintegration of the dihydroxypyrimidine ring in the spectrum, in addition to the ions that are usual for imidazothiazole systems.

EXPERIMENTAL

The mass spectra were recorded with an MKh-1303 spectrometer with direct introduction of the substances into the ion source at an ionizing voltage of 50 eV.

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