MASS SPECTRA OF DERIVATIVES OF IMIDAZO[2,1-b] THIAZOLE AND THIAZOLO[3,2-a]BENZIMIDAZOLE

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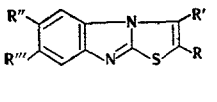
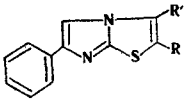
The mass spectra of 6-phenylimidazo[2,1-b]thiazole, thiazolo[3,2-a]benzimidazole, and a number of thiazole-ring-substituted derivatives were investigated. The fragmentation of both groups of compounds commences with cleavage of the bonds in the thiazole ring and leads to the appearance of nitrogen- and sulfur-containing fragments in the spectra. The common character of the mass spectrometric disintegration of the investigated compounds indicates that they have similar electronic structures. The mass number and position of a substituent in the thiazole ring can be determined on the basis of the mass numbers of a series of fragments.

The mass spectra of the simplest heteroaromatic compounds have been studied quite adequately [1], but the fragmentation of complex polycyclic structures, particularly condensed systems with a common nitrogen atom containing different heteroatoms, has been studied to a considerably lesser extent. These groups of substances include derivatives of imidazo[2,1-b]thiazole and thiazolo]3,2-a]benzimidazole. The mass spectra of only a few thiazolobenzimidazole derivatives have been described in the literature [2].

We have investigated the mass spectra of various thiazole-ring-substituted thiazolobenzimidazoles (I-XIV) and 6-phenylimidazothiazoles (XV-XVIII), the synthesis of which was described in [3, 4]. In order



I-XIV



XV-XVIII

I R=R′=R″=H; II R=CH_3, R′=R″=H; III R=R″=H, R′=CH_3; IV R=R′=CH_3, R″=H; V R=CH_3, R′=C_2H_5, R″=H; VI R=C_2H_5, R′=CH_3, R″=H; VII R=C_6H_5, R′=R″=H; VIII R=R″=H, R′=C_6H_5; IX R=R′=C_6H_5, R″=H; X R=CH_3, R′=C_6H_5, R″=H; XI R=$COCH_3$, R′=CH_3, R″=H; XII R=H, R′=C_6H_5, R″=CH_3; XIII R=R′=C_6H_5, R″=CH_3; XIV R=COC_6H_5, R′=H, R″=CH_3; XV R=R′=H; XVI R=H, R′=CH_3; XVII R=R′=CH_3; XVIII R=$COCH_3$, R′=H

to more accurately determine the fragmentation of the investigated compounds, we also recorded the spectra of a number of similar substituted 6,7-dimethylthiazolobenzimidazoles (XII-XIV).

The corresponding thiazole-ring-substituted thiazolobenzimidazoles and 6-phenylimidazothiazoles have approximately identical stabilities with respect to electron impact (W_m varies from 20 to 30% as a function of the substituent). In addition, it is characteristic that both classes of compounds were found to have common paths of mass-spectrometric disintegration. These facts can be considered as an indication of the closeness of the electronic structures of the condensed thiazolobenzimidazole system and the 6-phenylimidazothiazole system, in which the phenyl ring is in conjugation with the imidazothiazole ring.

Ions due to cleavage of the thiazole ring bonds are characteristic for both the thiazolobenzimidazoles and the 6-phenylimidazothiazoles. Peaks of $\overset{+}{S}\equiv CR$, the relative intensity of which reaches ~10%, and low-intensity peaks of the ions depicted below are observed in the spectra of unsubstituted I and XV and their derivatives (II-VII, XVI-XVIII):

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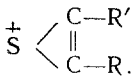
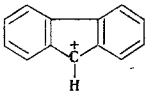


A comparison of the mass numbers of these ions makes it possible to determine a substituent and its position in the thiazole ring. Thus $\overset{+}{S}\equiv C-CH_3$ ions with m/e 59 are observed in the spectra of 2-methyl derivatives (II, IV, V, X, and XVII), while $\overset{+}{S}\equiv CH$ ions with m/e 45 observed in the spectra of the 2-unsubstituted compounds (see Table 1).

The $\overset{+}{S}\equiv C-C_6H_5$ ion peak in the spectrum of 2-phenylthiazolobenzimidazole is the most intense of all the fragmentary ions, while the intensity of the analogous $\overset{+}{S}\equiv CH$ (m/e 45) in the spectrum of the 3-phenyl isomer (VIII) is very low, and the most intense peak is that from the $[M-SCH\cdot]^+$ ion. This is evidence that the position of the phenyl group in the thiazole ring essentially determines the site of charge localization, and, in the case of VII, the charge is apparently localized on the sulfur atom.

The presence of $\overset{+}{C}H_2-C\equiv CR$ fragments (R = H, CH_3), which are produced by disintegration of the thiazole ring at the 1-2 and 3-4 bonds with migration of a hydrogen atom, proved to be typical for the spectra of II-IV, XVI, and XVII which have methyl substituents in the thiazole ring. Hydrogen migration occurs in this case apparently from the CH_3 group, inasmuch as this ion is absent in the spectra of I and XV, which do not have CH_3 groups, and in the spectra of the diphenyl and monophenyl derivatives (VII-X, XII-XIII). Cleavage of the C–N and C–S bonds without migration of a hydrogen atom to give $C_6H_5-C\equiv CR^+$ ions (R = H, C_6H_5) is characteristic for VII-X and XII-XIII.

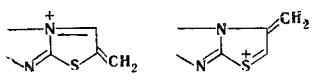
A distinctive feature of the disintegration of diphenyl derivatives IX and XIII is also the presence in the spectrum of an ion peak with mass number m/e 165, the intensity of which is second only to that of the molecular ion. In analogy with the disintegration of the diphenyl derivatives of imidzole, thiazole, and oxazole [5], structure A can be assigned to this ion.



A

The $[M-SH\cdot]^+$ ion is observed in the spectra of II-VI, X, XVI, and XVIII. The composition of this ion was established by an analysis of the high-resolution spectrum of XVI and on the basis of literature data [2]. A hydrogen atom is apparently stripped from the CH_3 group during this disintegration. This is attested to be the absence of the $[M-SH\cdot]^+$ ion in the spectra of diphenyl-substituted compounds (IX and XIII). Elimination of S rather than SH· from the molecular ion becomes more advantageous in the case of monophenyl-substituted VII, VIII, and XII, inasmuch as migration of a hydrogen atom to the sulfur atom is unlikely during the disintegration of these compounds.

Peaks of $[M-H\cdot]^+$ ions are characteristic for the spectra of II-IV and XVI. This ion peak is most intense (36%) for II; this is explained by the formation of stable fragment B. Stripping of a hydrogen atom in 3-methyl derivatives III and XVI gives stable structure C with charge localization on the sulfur atom, as in alkyl derivatives of thiophene [1].



B C

The low intensity of the $[M-H\cdot]^+$ ion in the spectra of III (13.8%) and XVI (9.1%) as compared with the intensity of $[M-H^{\cdot}]^+$ in II (36%) is apparently evidence that stabilization of the C type is less advantageous for imidazothiazole derivatives.

The ease of formation of ions B and C leads to the appearance of very intense $[M-CH_3^{\cdot}]^+$ peaks in the spectra of ethyl derivatives V and VI. As a consequence of the high advantageousness of stabilization with charge localization on the nitrogen atom (structure B), the intensity of the $[M-CH_3^{\cdot}]^+$ peak in VI is 2.5 times that of V.

TABLE 1. Mass Spectra of Derivatives of 6-Phenylimidazo[2,1-b]-thiazole and Thiazolo[3,2-a]benzimidazole

I 39 (6,5), 45 (6,8), 46 (2,6), 50 (6,7), 51 (7,1), 52 (2,3), 57 (3,3), 58 (7,3), 62 (2,7), 63 (7,6), 64 (5,6), 69 (2,3), 70 (3,8), 74 (2,7), 75 (9), 76 (8), 77 (2,3), 90 (6,8), 102 (21,2), 103 (6,1), 129 (24,2), 130 (2,4), 134 (3), 173 (2), 174 (100), 175 (13,7), 176 (5,6). $W_M = 34{,}7\%$

II 39 (9,4), 45 (4), 50 (5,7), 51 (6), 52 (2,3), 58 (2,1), 59 (9,1), 60 (2,8), 63 (6), 64 (4,5), 69 (2,1), 70 (2,1), 71 (3,6), 72 (2,8), 74 (2,3), 75 (7,2), 76 (7,6), 77 (3,8), 90 (8,1), 102 (15,3), 103 (3,8), 108 (2,3), 129 (14,5), 130 (4,7), 134 (6), 144 (2,1), 155(5), 160 (3), 161 (3,8), 187 (36,2), 188 (100), 189 (14,2), 190 (5,7). $W_M = 26{,}5\%$

III 39 (10,5), 40 (5,7), 44 (3), 45 (9), 50 (5,4), 51 (7), 52 (2,7), 63 (6), 64 (4,5), 69 (2,8), 70 (2,8), 71 (4,7), 73 (6,8), 74 (2), 75 (8,5), 76 (7,6), 77 (4,2), 90 (7), 102 (19), 103 (4,6), 116 (2,6), 117 (3), 118 (2,7), 134 (2,7), 143 (21,6), 155 (4,2), 160 (2), 187 (13,8), 188 (100), 189 (14), 190 (5,9). $W_M = 30{,}4\%$

IV 39 (7,4), 40 (7,7), 41 (4), 42 (3,1), 44 (3,4), 45 (3,4), 50 (4,3), 51 (6,8), 52 (2,5), 53 (6,3), 58 (2), 59 (6,3), 63 (4,9), 64 (3,4), 69 (2), 71 (2), 75 (6,3), 76 (4,9), 77 (3,1), 90 (7,7), 102 (13,5), 103 (2,3), 116 (2,3), 129 (2), 134 (7,4), 143 (13,7), 144 (3,4), 161 (2), 168 (3,7), 169 (5,7), 175 (4,9), 187 (19,7), 188 (2,8), 200 (2,5), 201 (27), 202 (100), 203 (9,7). $W_M = 27{,}5\%$

V 41 (2,5), 59 (2,8), 90 (3,8), 102 (4,3), 122 (2), 129 (3,3), 134 (4,1), 142 (2,1), 143 (13,2), 156 (2,1), 161 (2,1), 168 (2,3), 187 (6,1), 188 (2), 200 (4,5), 201 (54,5), 202 (9,9), 215 (5,6), 216 (100), 217 (13,9), 218 (5,1). $W_M = 34{,}5\%$

VI 39 (3,7), 41 (3,6), 45 (2,1), 51 (2,3), 53 (2), 63 (2,1), 69 (2), 75 (3), 76 (2,6), 77 (2), 90 (7,4), 101 (2), 102 (13,1), 103 (2,3), 107 (2,1), 108 (3,8), 115 (3,1), 116 (3,1), 129 (3), 131 (3), 134 (11,5), 142 (3,2), 143 (21,3), 144 (2,6), 156 (2), 161 (2), 168 (3), 175 (2,5), 187 (3,1), 199 (2,5), 200 (5,7), 201 (100), 202 (16,4), 203 (5,7), 215 (4,9), 216 (80,3), 217 (13,9), 218 (5,1). $W_M = 21\%$

VII 41 (2), 58 (2,1), 86 (10), 89 (2,9), 90 (3,6), 101 (2), 102 (4,4), 116 (3,6), 121 (14,4), 122 (3,2), 129 (4,1), 134 (1), 190 (2), 217 (2), 218 (4), 248 (3,2), 249 (5,1), 250 (100), 251 (20,5), 252 (6,5).

VIII 45 (1,5), 77 (3,6), 90 (2,1), 102 (3,9), 116 (1,3), 121 (1,7), 190 (1), 205 (5,8), 212 (2), 217 (1), 218 (2), 248 (7,3), 249 (5,5), 250 (100), 251 (22,3), 252 (7,4).

IX 42 (2), 43 (2,2), 44 (2,2), 53 (2), 58 (3), 77 (5,5), 86 (12,2), 91 (2,9), 101 (2,8), 102 (4,4), 103 (2,5), 121 (2,7), 149 (2,7), 163 (4,2), 165 (15,3), 166 (2,8), 177 (2), 178 (8,9), 179 (2), 190 (2), 205 (6,3), 250 (2,7), 266 (2), 325 (2,7), 326 (100), 327 (27,1), 328 (8,1).

X 45 (2,1), 77 (2,6), 90 (1), 102 (2), 103 (3), 104 (2), 116 (2), 115 (5,4), 134 (2), 187 (2,6), 204 (3,4), 205 (3,5), 212 (2), 231 (2,7), 237 (5,2), 261 (2), 262 (4,8), 263 (16,1), 264 (100), 265 (21,4), 266 (6,3).

XI 39 (11), 42 (2,2), 43 (2,8), 45 (7), 50 (5,1), 51 (8), 52 (2,9), 58 (3,7), 63 (6,6), 64 (4,9), 69 (4,8), 70 (5,1), 71 (3,6), 75 (9,5), 76 (8,6), 77 (3,6), 89 (2,7), 90 (10,4), 91 (2,2), 101 (2,2), 102 (31,3), 103 (4,8), 107 (2), 116 (3,5), 118 (2,2), 128 (2), 129 (2,8), 134 (5,2), 142 (2,4), 143 (65,1), 144 (9,4), 155 (2,4), 188 (14,6), 189 (13), 190 (2,7), 201 (3,6), 202 (1,4), 215 (67,5), 216 (10), 230 (100), 236 (19). $W_M = 17{,}8$

XII 45 (2), 77 (2,8), 91 (2,4), 102 (2), 103 (2,2), 116 (2), 117 (2), 134 (2,2), 139 (3,7), 176 (2), 261 (2,2), 262 (2,1), 263 (14,9), 264 (3), 277 (27,9), 278 (100), 279 (3,1), 280 (6,9).

XIII 77 (1,5), 165 (3,8), 177 (3,4), 178 (4,4), 340 (7,2), 341 (2,1), 352 (4,4), 353 (21,2), 354 (100), 355 (29), 356 (6,1).

XIV 44 (2,4), 77 (18), 78 (2), 105 (27), 106 (2,5), 157 (4), 201 (3,9), 229 (2,2), 277 (2), 291 (8,8), 292 (2,1), 304 (3,6), 305 (20), 306 (100), 307 (20), 308 (7,3).

XV 39 (4), 40 (2,8), 44 (5,1), 45 (3,8), 50 (3), 51 (5,5), 52 (2,8), 57 (1,9), 58 (4,2), 59 (2,1), 63 (4,4), 64 (2,5), 70 (3,2), 75 (2,8), 76 (4,9), 77 (5,1), 87 (2,5), 88 (2,1), 89 (5,8), 90 (3,6), 101 (2,6), 102 (6,2), 103 (8,1), 115 (4,4), 116 (9,5), 128 (4,7), 129 (2,3), 142 (2,6), 147 (2,8), 155 (2), 173 (2), 174 (3), 175 (3), 198 (3), 199 (10,), 200 (100), 201 (14,5), 202 (5,8). $W_M = 30{,}3\%$

XVI 39 (9,3), 45 (5,7), 50 (2,6), 51 (6), 52 (2,4), 63 (4,3), 71 (5,4), 72 (2), 75 (2,3), 76 (5,4), 77 (7,7), 89 (5,9), 90 (3,1), 101 (2,6), 102 (7,7), 103 (12,6), 104 (2,6), 115 (2,7), 116 (8,1), 117 (5,7), 128 (6), 142 (3,4), 146 (2), 147 (5,4), 148 (2), 169 (3,2), 174 (2), 175 (2), 212 (2,3), 213 (9,1), 214 (100), 215 (14,3). $W_M = 31{,}7\%$

XVII 39 (7,1), 40 (2,1), 41 (2,1), 45 (3), 51 (5,1), 52 (2), 53 (6,9), 59 (4,6), 63 (3), 71 (3,4), 76 (4,2), 77 (6,3), 89 (4,6), 90 (2), 101 (2,2), 102 (6,7), 103 (10), 104 (3,1), 115 (2,6), 116 (6,4), 117 (5), 127 (2), 128 (6,8), 129 (2), 147 (2,9), 148 (2), 154 (2,6), 168 (2), 169 (3), 170 (2), 175 (2), 195 (2), 213 (2,5), 226 (3,7), 227 (17,6), 228 (100), 229 (19,2), 230 (6,6). $W_M = 30{,}4\%$

XVIII 39 (12,4), 40 (7,1), 41 (2,6), 42 (3,5), 43 (23,2), 44 (8,4), 51 (5,8), 52 (3,5), 59 (8,9), 63 (3,5), 71 (2,6), 76 (4,9), 77 (8,4), 89 (7,6), 90 (2,6), 91 (2,6), 101 (3,1), 102 (8,9), 103 (9,8), 104 (4), 114 (2,6), 115 (3,5), 116 (8,4), 117 (7,1), 119 (2,2), 130 (7), 132 (4), 134 (4), 147 (2,6), 154 (2,6), 155 (2,5), 169 (9,8), 170 (2,5), 183 (5), 213 (12,9), 214 (6,2), 241 (3,2), 242 (5,5), 243 (2,7), 255 (8,9), 256 (100), 257 (21), 258 (6). $W_M = 22{,}1\%$

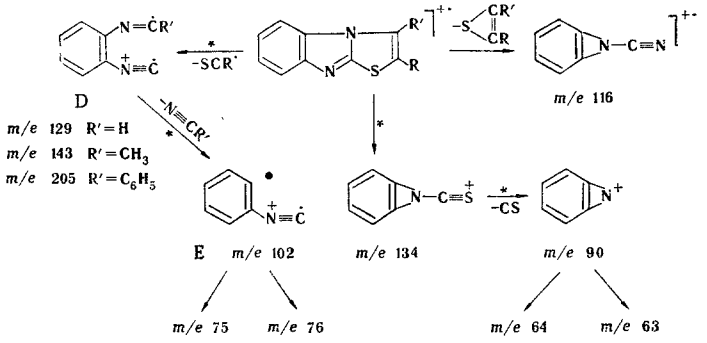
An intense $[M-H^{\cdot}]^+$ ion, to which structures B and C should be assigned, is also observed in the spectra of 2,3-dimethyl derivatives IV and XVII. However, $[M-CH_3^{\cdot}]^+$ ion peaks are observed in addition to $[M-H^{\cdot}]^+$ ion peaks in the spectra of IV and XVII. It might be assumed that this ion is formed via the disintegration mechanism peculiar to dimethyl derivatives of thiazole [6]. In the systems that we examined, the charge may be localized both on the sulfur atom and on the nitrogen atom. Stripping of a CH_3 group

from both the 2 position and the 3 position of the thiazole ring is therefore possible, as a consequence of which the $[M-CH_3^{\cdot}]^+$ ion may have structures B and C.

It should be noted that while the intensity of the $[M-CH_3^{\cdot}]^+$ ion is only 2.5% for XVII and approaches the intensity of the analogous ion in the spectra of thiazole derivatives, stripping of a methyl group in IV is a very advantageous process, and the intensity of the $[M-CH_3^{\cdot}]^+$ ion reaches 19.7%.

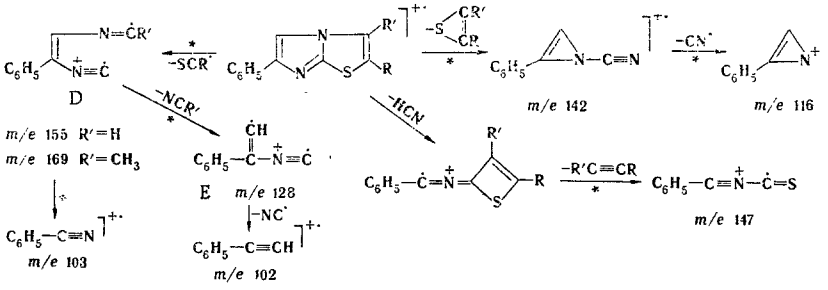
Ions obtained by stripping of sulfur-containing neutral fragments are observed in addition to the above-examined fragments in the spectra of thiazolobenzimidazoles.

Ion D, which is formed by the elimination of SCR$^{\cdot}$ from the molecular ion, and ion E, which is produced during its disintegration, have the greatest intensities of all the fragmentary ions. Moreover, the intensity of D is substantially higher than the intensity of the SCR ion. This once again indicates the advantageousness of charge localization on the nitrogen atom and removal of SCR$^{\cdot}$ as a neutral fragment.



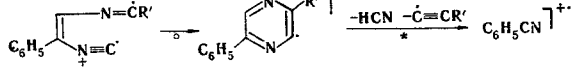
The magnitude of the mass number of ion D and of ion $\overset{+}{S}CR^{\cdot}$ makes it possible to determine the position of a substituent in the thiazole ring of the investigated heterocycles.

Similar fragmentation of phenylimidazothiazole derivatives is presented below. The compositions of the fragments were established by investigation of the high-resolution spectrum of XVI.



It can be seen from a comparison of the spectra of 6-phenylimidazothiazoles and thiazolobenzimidazoles that the principal paths of their disintegration are identical and are due to cleavage of the thiazole ring bonds. At the same time, the change in the mode of attachment of the phenyl group to the thiazole ring in the case of 6-phenyl-substituted imidazothiazoles leads to a decrease in the relative intensities of the D and E ions and to the appearance of low-intensity $[M-HCN]^{+\cdot}$ ions, which can be explained by elimination of HCN from the imidazole rings.

The $[C_6H_5-C\equiv N]^{+\cdot}$ ion, with an intensity of 13%, is also observed in the spectra of 6-phenylimidazothiazole. Its production from ion E, as attested to by the presence of the corresponding metastable peak, can be explained by skeletal rearrangement of ion E prior to disintegration.



A characteristic peculiarity of the fragmentation of 6-phenylimidazothiazole derivative is the absence of $[M-C_6H_5^{\cdot}]^+$ ions and the low intensity of the ion with m/e 77; this proves the high degree of conjugation of the phenyl group with the imidazole ring in the investigated system.

The introduction of an acetyl group into the 2 position (XI, XVIII) brings about only slight changes in the basic principles of the disintegration of compounds of these classes. In addition to the $COCH_3^+$ ion, intense $[M-CH_3^{\cdot}]^+$ and $[M-COCH_3^{\cdot}]^+$ ion peaks appear in the spectra. Subsequent elimination of CS from

the $[M-COCH_3^{\cdot}]^+$ ion leads to the known D ion. The relatively low stability of the $[M-COCH_3^{\cdot}]^+$ ion as compared with the molecular ions of the compounds examined above increases the probability of the formation of ion D, as a consequence of which its intensity reaches 65%, and the intensity of the fragment produced during its disintegration increases correspondingly. It should be noted that the formation of $[M-CO]^{+\cdot}$ ions, which are so typical for the spectra of C-acetyl and benzoyl derivatives of benzimidazole [7], is not characteristic for any of the examined acetyl derivatives of 6-phenylimidazothiazole and thiazolylbenzimidazole.

Thus an examination of the mass spectra showed that the fragmentation of the imidazothiazole system commences primarily through cleavage of the thiazole ring bonds, regardless of whether this system is condensed with a benzene ring or is in the 6 position. This sort of character of the disintegration is apparently explained by the fact that the weakest link in the described systems is the thiazole ring. This also leads to the monotypic character of the mass-spectrometric fragmentation of the two groups of compounds examined in this paper.

EXPERIMENTAL

The mass spectra were obtained with an MKh-1303 spectrometer with direct introduction of the sample into the source. The ionizing voltage was 50 eV. The high-resolution spectra were recorded at our request with a JMS-01 (sG-2) spectrometer in the mass spectrometric center of JEOL (Japan), for which the authors are sincerely grateful.

LITERATURE CITED

1. G. Budzikiewicz, C. Djerassi, and D. Williams, Interpretation of the Mass Spectra of Organic Compounds [Russian translation], Mir, Moscow (1966).
2. H. Ogura, T. Ltoh, and K. Kikuchi, J. Heterocycl. Chem., 6, 797 (1969).
3. P. M. Kochergin and M. N. Shchukina, Zh. Obshch. Khim., 26, 458 (1956).
4. A. N. Krasovskii and P. M. Kochergin, Khim. Geterotsikl. Soedin., 899, 321 (1967).
5. I. H. Bowie, P. F. Donaghue, H. I. Rodda, and B. K. Simons, Tetrahedron, 24, 3965 (1968).
6. R. A. Khmel'nitskii, E. A. Kunina, S. L. Gusinskaya, and V. Yu. Telly, Khim. Geterotsikl. Soedin., 1372 (1971).
7. I. H. Bowie and J. R. Cooks, Tetrahedron, 24, 1875 (1968).