MASS-SPECTROMETRIC STUDY OF THE RING—CHAIN TAUTOMERISM OF S- and N-ACYLALKYL-2-MERCAPTOBENZIMIDAZOLE DERIVATIVES

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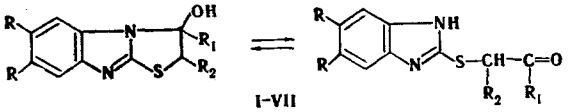
The mass spectra of a number of S- and N-acylalkyl derivatives of 2-mercaptobenzimidazole were studied in order to investigate the ring—chain tautomerism of compounds of this group. It is shown that the fragmentation of the investigated compounds takes place from the open form of the molecular ion. The data obtained in this study are compared with the results of studies of the tautomeric equilibria in very dilute solutions. The principal fragmentation regularities were established.

Attempts to use mass-spectrometric data for the investigation of tautomeric equilibria have been made in recent years. The keto—enol equilibrium of acetylacetone [1,2] and the ring—chain tautomerism of oxazolidine derivatives [2] have been studied by means of mass spectrometry.

In this connection, a mass-spectrometric study of S- and N-acylalkyl derivatives of 2-mercaptobenzimidazole — compounds for which the existence of ring—chain tautomerism in solution has been demonstrated [3] —seemed of substantial interest.



I-VII

VIII-IX

Compounds with the following substituents were subjected to mass-spectrometric investigation:

I $R = R_1 = R_2 = H$; II $R = R_1 = H$, $R_2 = CH_3$; III $R = R_2 = H$, $R_1 = C_6H_5$; IV $R = H$, $R_1 = R_2 = C_6H_5$; V $R = CH_3$, $R_1 = R_2 = H$; VI $R = R_2 = CH_3$, $R_1 = H$; VII $R = R_1 = CH_3$, $R_2 = H$; VIII $R = CH_3$; IX $R = C_6H_5$.

An examination of the IR and NMR spectra of these substances [3] made it possible to conclude that III, IV, VIII, and IX exist in the open form in dilute chloroform solutions and in the solid state, whereas I, II, and V-VII exist as mixtures of the ring and chain forms under these conditions. The concentration of the open form is higher in solution than in the crystalline state.

In mass-spectrometric investigations the substance exists in the gas phase at high rarefaction, in which state collisions between the molecules are practically absent. These conditions differ substantially from the conditions in the condensed phase (solutions and

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crystals) under which the IR and NMR spectra are measured. The results obtained during a mass-spectrometric study of the indicated group of compounds therefore could substantially supplement the available data on their ring—chain tautomerism and primarily give information under gas-phase conditions at high temperatures.

From the structure of the molecules one might assume that elimination of an OH group from the molecular ion and subsequent stabilization of the charge on the common nitrogen atom and also elimination of a water molecule to give an ion having the structure of the corresponding thiazolo[1,2-a]benzimidazole derivative should be characteristic for the fragmentation of the chain form. The subsequent fragmentation of this ion should give a spectrum coinciding with the spectrum of the thiazolo[1,2-a]benzimidazole derivative [4].

The spectrum of the open form should be characterized by stepwise fragmentation of the side chain. Cleavage of the bonds in the α position relative to the sulfur atom should be considered to be a particularly favorable fragmentation pathway.

Peaks of $[M - H_2O]^{+\cdot}$ and $[M - OH]^{+\cdot}$ ions are absent in the spectra of all of the investigated compounds, and the spectra are satisfactorily interpreted on the basis of the notion of fragmentation of the molecular ion only from the open form. There are two reasons for this: first, a shift in the tautomeric equilibrium to favor the open form during vaporization of the substance and, second, conversion of the already excited molecular ion to the open form immediately prior to fragmentation.

In connection with an examination of these assumptions, we studied the IR spectra of ∿0.004% solutions of I, II, and V-VII in carbon tetrachloride*. It was observed that in markedly dilute solutions the concentration of the open form increases sharply even for I and V, which in the crystalline form exist principally in the chain form [3]. Evidence for this offered by the appearance in the spectra of the solutions of an intense band at 1730 cm^{-1} corresponding to CO stretching vibrations. Heating the solutions also shifts the equilibrium to favor the open form. The change in the ratio of the intensities of the bands at 3580 (ν_{OH}), 3460 (ν_{NH}), and 1730 cm^{-1} (ν_{CO}) in the spectrum of a dilute solution of VII in carbon tetrachloride as the temperature is changed from 30 to 70° is presented in Fig. 1. Similar changes are also observed in the spectra of a solution in chloroform. The shift in the equilibrium provides a basis for the assumption that the investigated substances exist in the open form in the gas phase at high temperatures, and this is also responsible for the similar forms of the molecular ions.

It is interesting to note that ion peaks evidently belonging to the products of thermal dehydration of the substances appear in the spectra of I, II, and V-VII after samples of these compounds have remained for a long time in the spectrometer. Evidence for this is provided by the irreversible decrease in the intensity of the molecular ion peak and the appearance and increase in intensity of the $[M - H_2O]^{+\cdot}$ ion when the sample is heated. This provides a basis for the assumption that, prior to vaporization, the indicated substances may

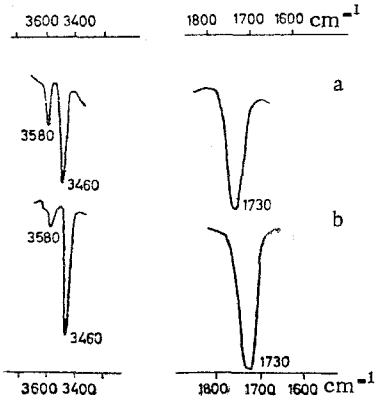
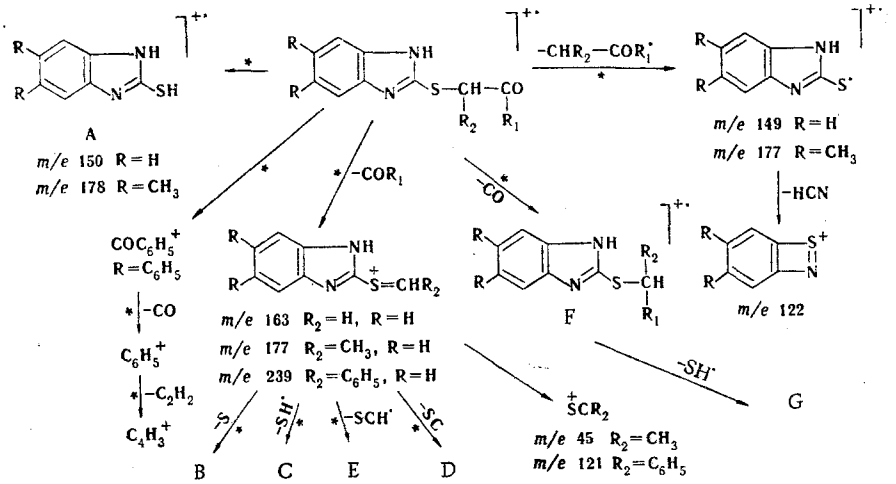


Fig. 1. IR spectra of a 0.004% solution of VII in CCl_4: a) at 30°; b) at 70°.

*It did not seem possible to obtain the IR spectra in the gas phase because of the low volatilities of the investigated compounds.

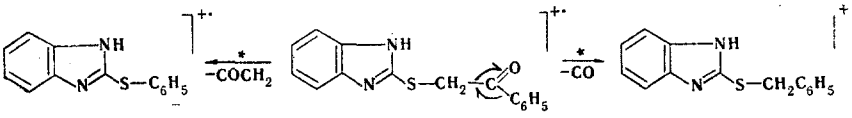
undergo thermal decomposition due to dehydration of the chain form. The appearance of the ions of the dehydration product is not observed in the spectra of phenyl-substituted III and IV, which exist only in the open form in the solid phase.

Judging from the spectra, the fragmentation of I-VII is realized via the pathways presented in the following scheme:



Elimination ofthe COR_1 group and formation of ion A proved to be the most favorable pathway of fragmentation of the molecular ions. Rearrangement processes with elimination of S, SH, SC, SCH, and CO from the side chain were observed in the spectra of all of the investigated compounds. The compositions and structures of the ions were proved by the presence of the corresponding metastable transitions and by analysis of the high-resolution spectra of I and the spectrum of deuterium-substituted III.

Elimination of CO and CH_2CO from the molecular ion is observed in the spectrum of III:

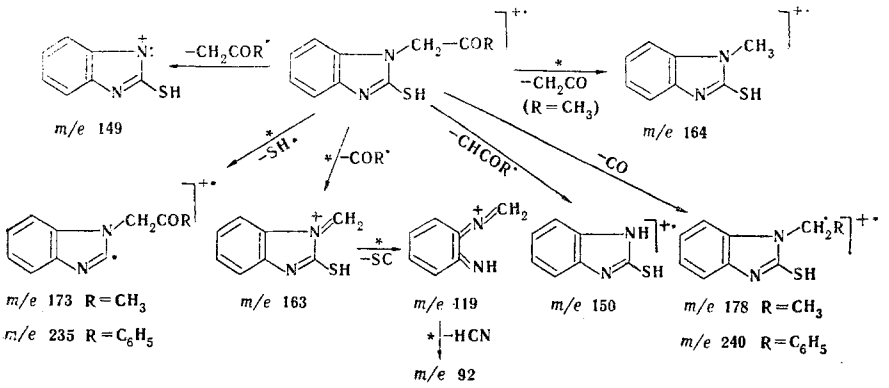


This explains the appearance of a tropylium ion peak (m/e 91) and peaks of its fragmentation products, in addition to the above described fragments, in the spectrum of derivative III. Similar elimination of CO is also observed in the spectra of benzoyl derivatives IV and IX. This sort of rearrangement has been previously described for 2-benzoylbenzimidazole [4].

An intense peak with a mass number of 150, to which the peak with m/e 178 corresponds in the spectra of V-VII, is observed in the spectra of I-IV and VIII-IX. On the basis of data from the high-resolution spectrum of I and a comparison of the spectra of compounds with different substituents, the ion A structure was assigned to this ion. The intensity of this peak increases irreversibly on prolonged heating of phenyl derivatives III and IV, which exist only in the open form in the solid phase. This provides a basis for the assumption that the ion with m/e] 150 may be observed as a consequence of fragmentation of the investigated compounds and as the molecular ion of the product of thermal decomposition of the open form of the substance.

In the case of III and, probably, IV, the peak with m/e 150 belongs to two ions. Evidence for this is provided by the fact that this peak is retained along with the appearance of an ion with m/e 151 in the spectrum of deuterium-substituted III. It might be assumed that the $S{=}CH{-}C\langle^{O}_{C_6H_5}$ ion, which does not include a labile amino group hydrogen, is formed in addition to the ion with structure A.

As in the case of the above-described S-derivatives, the fragmentation of N-acylalkyl derivatives VIII and IX proceeds from the open form via the following scheme:



Thus the investigated 2-mercaptobenzimidazole derivatives undergo fragmentation from the open form of the molecular ion, and this is evidently explained by the marked shift of the equilibrium to favor the open form as the substances pass into the gas phase. Fragmentation proceeds with primary cleavage of the bonds in the side chain and is characterized by rearrangement processes with elimination of CO, SCH, SC, and S.

Mass Spectra of the Investigated Compounds*

I 39 (8), 44 (3), 45 (7), 51 (3), 63 (10), 64 (10), 65 (4), 77 (10), 78 (4), 90 (21), 91 (16), 92 (7), 102 (3), 104 (4), 105 (8), 117 (6), 118 (25), 119 (24), 122 (18), 129 (4), 131 (41), 132 (6), 134 (6), 149 (13), 150 (81), 151 (9), 152 (4), 163 (44), 164 (15), 174 (5), 175 (10), 191 (10), 192 (100), 193 (13), 194 (6)

II 39 (6), 45 (4), 51 (2), 57 (6), 59 (5), 63 (7), 64 (6), 65 (7), 77 (5), 90 (16), 91 (11), 92 (7), 102 (3), 105 (4), 118 (30), 119 (14), 122 (20), 145 (50), 146 (7), 149 (16), 150 (78), 163 (19), 177 (25), 178 (7), 189 (4), 206 (100), 207 (15), 208 (6)

III 39 (4), 41 (3), 43 (6), 44 (4), 45 (10), 51 (10), 63 (3), 65 (5), 77 (54), 78 (8), 90 (4), 91 (9), 105 (100), 106 (11), 118 (5), 119 (5), 120 (6), 122 (11), 134 (3), 149 (6), 150 (20), 163 (34), 226 (7), 240 (4), 268 (12), 269 (2)

IV 39 (9), 51 (16,0), 52 (3), 63 (5), 65 (9), 75 (3), 77 (16), 78 (5), 89 (3), 90 (4,0), 91 (8), 105 (100), 106 (13), 118 (3), 121 (9), 122 (4), 149 (3), 150 (13), 152 (4), 165 (7), 166 (2), 167 (7), 196 (2), 201 (3), 202 (3), 207 (6), 239 (25), 240 (5), 344 (14), 345 (4)

V 41 (4), 42 (4), 43 (4), 44 (4), 45 (5), 51 (3), 52 (2), 53 (2), 57 (2), 64 (2), 65 (7), 76 (2), 77 (6), 78 (4), 79 (2), 89 (4), 90 (4), 91 (15), 92 (8), 94 (2), 96 (6), 97 (2), 102 (2), 103 (4), 104 (3), 105 (2), 116 (6), 117 (10), 118 (6), 119 (2), 120 (4), 121 (6), 122 (3), 131 (8), 132 (4), 141 (3), 144 (3), 145 (10), 146 (4), 147 (10), 148 (3), 149 (4), 150 (8), 152 (4), 156 (3), 157 (4), 158 (4), 159 (44), 160 (12), 161 (6), 176 (5), 177 (18), 178 (63), 179 (11), 180 (4), 190 (9), 191 (39), 192 (16), 193 (3), 202 (3), 203 (7), 219 (4), 220 (100), 221 (32), 222 (9)

VI 42 (7), 91 (12), 92 (3), 108 (3), 131 (3), 145 (3), 146 (5), 147 (3), 150 (2,0), 173 (48,0), 174 (7), 177 (9), 178 (51), 179 (10), 180 (3), 191 (10), 205 (15), 206 (7), 217 (3), 233 (3), 234 (100), 235 (17), 234 (6)

VII 41 (7), 42 (10), 43 (100), 44 (4), 45 (13), 51 (7), 52 (4), 53 (4), 58 (10), 65 (10), 66 (3), 75 (4), 77 (9), 85 (3), 89 (5), 90 (8), 91 (20), 92 (12), 103 (11), 104 (5), 105 (2), 116 (7), 117 (6), 118 (6), 120 (3), 131 (7), 132 (4), 145 (8), 146 (7), 147 (16), 148 (3), 150 (9), 157 (3), 159 (43), 160 (9), 162 (3), 163 (3), 176 (2), 177 (20), 178 (9), 190 (2), 191 (80), 192 (25), 193 (7), 194 (2), 216 (5), 217 (2), 219 (4), 234 (41), 235 (8), 236 (3)

VIII 39 (3), 40 (30), 43 (19), 44 (6), 45 (12), 46 (5), 51 (8), 65 (4,5), 76 (4), 77 (21), 78 (6), 83 (4), 90 (5), 91 (5), 92 (6), 102 (5), 103 (3), 104 (4), 105 (16), 106 (2), 109 (2), 111 (2), 118 (8), 119 (36), 120 (4), 122 (4), 129 (8), 130 (3), 131 (13), 132 (5), 134 (5), 135 (3), 149 (5), 156 (6), 163 (79), 164 (46), 165 (10), 166 (3), 173 (9), 174 (2), 189 (2), 206 (100), 207 (16), 208 (6)

IX 42 (3), 43 (6), 44 (9), 45 (6), 51 (7), 55 (2), 56 (2), 57 (2), 64 (2), 65 (3), 73 (4), 77 (46), 78 (6), 90 (3), 91 (6), 92 (4), 102 (4), 103 (2), 104 (2), 105 (100), 106 (9), 118 (4), 119 (20), 120 (4), 122 (3), 129 (4), 134 (4), 149 (4.5), 150 (3), 163 (50), 164 (7), 165 (3), 207 (2), 236 (3), 240 (2), 268 (66), 269 (14), 270 (5)

*The peaks with relative intensities lower than 1% are not presented.

EXPERIMENTAL

The low-resolution mass spectra were obtained with an MKh-1303 spectrometer with direct introduction of the samples into the source. The ionizing-electron energy was 50 eV. The ionization chamber temperature was 125°. The high-resolution mass spectrum was obtained with

a JMS-01-SG-2 spectrometer. The authors thank co-workers of the All-Union Scientific-Research Institute of Vitamins Zh. K. Torosyan and V. A. Zamureenko for making these measurements. The IR spectra of carbon tetrachloride solutions of the compounds at 30 to 70° were recorded with Perkin—Elmer 457 and UR-10 spectrometers.

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STUDY OF CONDENSED PYRIMIDINE, PYRAZINE, AND PYRIDINE SYSTEMS.

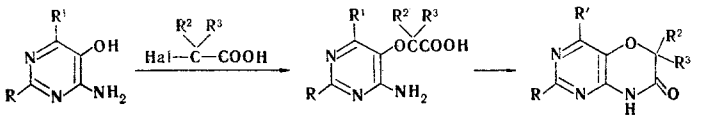
XXXIV*. SYNTHESIS AND PROPERTIES OF PYRIMIDO[5,4-b][1,4]OXAZIN-7-ONES

N. V. Sazonov and T. S. Safonova

UDC 547.856'867.07

A new method was developed for the synthesis of pyrimido[5,4-b][1,4]oxazin-7-ones by O-alkylation of 5-hydroxy-6-aminopyrimidines with α-halo carboxylic acids and subsequent cyclization of the resulting pyrimdyloxyacetic acids in acetic anhydride. The reaction of chloropyrimidooxazinones with hydrazine gives the corresponding hydrazinopyrimidooxazinones, from which the azides were obtained. Unsubstituted pyrimido[5,4-b][1,4]oxazin-7-one was synthesized.

It has been observed that the reaction of 2-methyl-4-chloro-5-hydroxy- (I) and 2-methyl-4,6-dihydroxy-6-aminopyrimidine (II) with chloroacetic acid in water in the presence of alkali gives, after acidification, 6-amino-5-pyrimidyloxyacetic acids (IV, V).



I-III IV-VII IX-XXI

I R=CH_3, R^1=Cl, II R=CH_3, R^1=OH, III R=H, R^1=Cl, IV R=CH_3, R^1=Cl, R^2=R^3=H, V R=CH_3, R^1=OH, R^2=R^3=H, VI R=CH_3, R^1=Cl, R^2=C_2H_5, R^3=H, VII R=CH_3, R^1=Cl, R^2=C_3H_7, R^3=H, IX R=CH_3, R^1=Cl, R^2=R^3=H, X R=CH_3, R^1=OH, R^2=R^3=H, XI R=R^2=CH_3 R^1=Cl, R^3=H, XII R=CH_3, R^1=Cl, R^2=C_2H_5, R^3=H, XIII R=CH_3, R^1=Cl, R^2=C_3H_7, R^3=H, XIV R=R^2=R^3=CH_3, R^1=Cl, XV R=R^3=H, R^1=Cl, R^2=CH_3, XVI R=R^3=H, R^1=Cl, R^2=C_2H_5, XVII R=R^2=H, R^1=Cl, R^2=C_3H_7, XVIII R=H, R^1=Cl, R^2=R^3=CH_3, XIX R=R^2=CH_3, R^1=OH, R^3=H, XX R=CH_3, R^1=OH, R^2=C_2H_5, R^3=H, XXI R=R^2=R^3=CH_3, R^1=OH

*See [1] for communication XXXIII.

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