MASS SPECTRA AND STRUCTURE OF HALO-SUBSTITUTED 2- and 4-AMINOPYRIMIDINES

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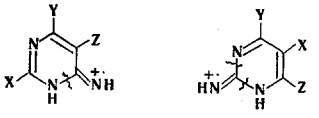
The mass spectra of methyl- and halo-substituted 2- and 4-aminopyrimidines at an ionizing electron energy of 70 eV were studied. It is shown that the molecular ion of the investigated compounds corresponds primarily to the imine form. This structure determines the principal direction of disintegration, which proceeds through the formation of pseudomolecular ions with an imidazole or pyrazole structure, depending on the position of the amino group in the pyrimidine ring.

In a continuation of our investigations of pyrimidine systems [1], we have studied the mass spectra of 4-amino-2-methylpyrimidine (I), 4-amino-2-chloropyrimidine (II), 4-amino-2-chloro-6-methylpyrimidine (III), 4-amino-5-bromo-6-methylpyrimidine (IV), 4-amino-2,6-dichloropyrimidine (V), 2-amino-5-chloropyrimidine (VI), 2-amino-5-bromopyrimidine (VII), and 2-amino-4,6-dichloropyrimidine (VIII). The mass spectra of I-VI have not been described in the literature.

The mass spectra were recorded with a Varian MAT-CH-6 spectrometer with direct introduction of the substance into the ion source at an ionization-chamber temperature of 180°C and an ionizing voltage of 70 eV.

The mass spectra of the investigated compounds and the resistances (W_M) of the molecules to electron impact, which are the ratios of the intensities of the peaks of the polyisotopic molecular ion to the total current in percent, are presented in Table 1.

Correlation of the experimental and literature data [2, 3] with respect to the dissociative ionization of halo- and methyl-substituted 2- and 4-aminopyrimidines makes it possible to suppose that the molecular ion exists chiefly in the imine form, which, as a rule, also determines the principal directions of disintegration.



In this case, cleavage of the bond between the ring heteroatom and the carbon bonded to the imine group is most likely.

For halo-substituted 4-aminopyrimidines (Table 2) the overall intensity of the ions formed during cleavage of the HNC−N bond (ΣI_{3-4}) is 21-53% of the total current. It should be noted that these values are, respectively, 31.6, 48.0, and 31.3 for I, 4-amino-6-methylpyrimidine, and 4-amino-2,6-dimethylpyrimidine (calculated from the literature data).

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TABLE 1. Mass Spectra of the Investigated Compounds*

4-Amino-2-methylpyrimidine

26 (10,7), 27 (12,8), 29 (8,8), 38 (6,7), 39 (14,8), 40 (17,3), 41 (44,4), 42 (27,2), 43 (23,5), 45 (3,1), 47 (4,5), 51 (6,1), 52 (14,3), 53 (7,3), 54 (6,3), 55 (10,7), 56 (3,9), 57 (7,8), 65 (4,3), 66 (11,2), 67 (27,5), 68 (25,0), 69 (16,0), 70 (4,7), 71 (4,7), 73 (4,3), 77 (3,1), 78 (4,7), 79 (4,5), 81 (12,4), 82 (27,0), 83 (19,9), 85 (11,7), 91 (3,1), 92 (6,1), 93 (15,3), 94 (6,9), 95 (6,1), 96 (4,7), 97 (4,1), 108 (3,7), 109 (100,0), 110 (17,9), 111 (2,7). $W_M = 16{,}8$.

4-Amino-2-chloropyrimidine

26 (11,0), 27 (5,3), 38 (5,6), 39 (8,9), 40 (31,8), 41 (40,0), 42 (10,1), 43 (8,8), 51 (7,8), 52 (15,2), 53 (9,6), 62 (7,4), 66 (9,4), 67 (40,0), 68 (5,0), 94 (58,7), 95 (4,6), 102 (29,4), 104 (9,8), 129 (100,0), 130 (6,2), 131 (34,1), 132 (2,2). $W_M = 19{,}7$.

4-Amino-2-chloro-6-methylpyrimidine

38 (6,1), 39 (18,6), 40 (16,8), 41 (23,3), 42 (13,2), 43 (26,2), 52 (4,0), 53 (4,0), 54 (8,9), 62 (6,1), 65 (4,8), 66 (22,2), 67 (38,8), 68 (8,9), 81 (4,0), 108 (30,1), 116 (21,5), 118 (7,2), 143 (100,0), 144 (7,3), 145 (29,1), 146 (2,7). $W_M = 23{,}0$.

4-Amino-5-bromo-6-methylpyrimidine

26 (7,0), 27 (10,8), 30 (5,4), 37 (9,6), 38 (19,5), 39 (25,5), 40 (14,0), 41 (7,0), 42 (26,8), 43 (14,0), 51 (7,7), 52 (13,4), 53 (10,8), 54 (21,0), 55 (3,2), 63 (3,5), 64 (7,7), 65 (8,9), 68 (25,5), 67 (22,3), 68 (3,5), 79 (3,8), 80 (5,4), 81 (38,3), 82 (3,8), 91 (3,2), 93 (3,8), 107 (6,7), 108 (55,8), 109 (5,1), 117 (3,8), 118 (7,0), 119 (25,8), 120 (8,6), 121 (17,9), 130 (3,2), 131 (3,5), 132 (3,8), 145 (4,5), 147 (5,1), 160 (13,4), 162 (12,8), 187 (100,0), 188 (8,3), 189 (100,0). $W_M = 13{,}7$.

4-Amino-2,6-dichloropyrimidine

26 (4,0), 27 (5,8), 30 (4,7), 31 (4,4), 35 (3,6), 38 (11,7), 39 (18,6), 40 (31,3), 41 (16,4), 42 (6,9), 43 (5,8), 45 (3,3), 47 (5,8), 51 (14,2), 53 (7,3), 60 (8,7), 61 (3,6), 62 (17,5), 64 (8,0), 65 (8,0), 66 (24,8), 67 (78,6), 68 (9,1), 74 (9,5), 76 (4,7), 77 (4,4), 86 (10,2), 87 (4,7), 88 (4,0), 92 (23,3), 93 (3,6), 101 (5,5), 128 (56,5), 129 (4,4), 130 (21,1), 136 (42,3), 137 (3,3), 138 (28,1), 140 (5,8), 163 (100,0), 164 (5,8), 165 (62,3), 166 (4,0). $W_M = 13{,}7$.

2-Amino-5-chloropyrimidine

26 (3,0), 27 (5,6), 38 (6,9), 39 (7,2), 40 (7,9), 42 (16,0), 43 (9,5), 47 (6,1), 51 (10,7), 52 (10,9), 53 (5,9), 60 (16,0), 62 (5,3), 66 (4,9), 67 (41,9), 73 (3,6), 74 (11,8), 75 (20,9), 76 (5,3), 77 (7,6), 94 (22,4), 101 (5,1), 102 (32,3), 104 (11,2), 129 (100,0), 130 (6,2). $W_M = 21{,}9$.

2-Amino-5-bromopyrimidine

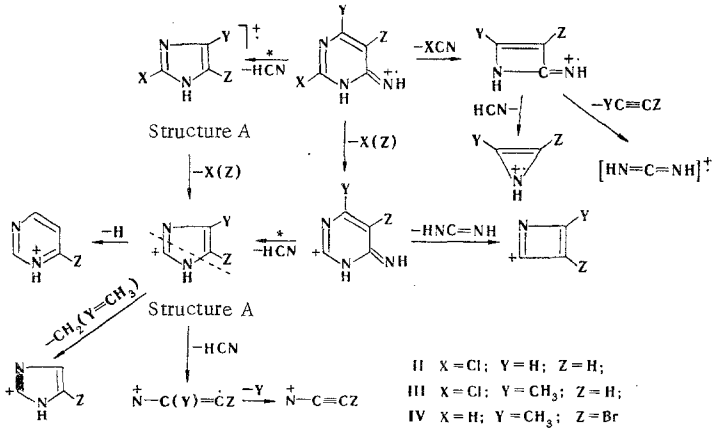
26 (3,4), 27 (5,2), 38 (4,4), 39 (4,4), 40 (9,2), 42 (8,2), 43 (7,5), 51 (6,8), 52 (9,6), 66 (6,0), 67 (39,0), 94 (24,7), 95 (5,6), 104 (7,8), 106 (7,3), 118 (4,9), 119 (5,5), 121 (5,8), 146 (8,1), 148 (7,0), 173 (96,1), 174 (6,2), 175 (100,0), 176 (6,6). $W_M = 21{,}7$.

2-Amino-4,6-dichloropyrimidine

27 (4,9), 38 (11,1), 39 (12,8), 40 (10,8), 42 (7,7), 43 (23,8), 47 (4,6), 51 (13,1), 52 (4,9), 53 (7,7), 60 (4,3), 62 (11,4), 64 (5,3), 65 (10,7), 66 (10,8), 67 (40,9), 68 (3,7), 74 (6,5), 86 (11,0), 88 (4,2), 92 (33,3), 128 (100,0), 129 (8,7), 130 (33,3), 163 (69,7), 164 (4,2), 165 (48,5), 166 (3,4). $W_M = 12{,}0$.

*The intensities of peaks that are greater than 3% of the maximum are presented.

The disintegration of the halo-substituted 4-aminopyrimidines can be represented by the following general scheme:*



*Here and elsewhere, the number under the formula corresponds to the mass number of the ion, while the number in parentheses is the intensity of the given peak in percent of the total ion current; the asterisk indicates the presence of the corresponding metastable process.

TABLE 2. Characteristic Ions Formed in the Dissociative Ionization of Halo-Substituted 4-Aminopyrimidines*

Ions	Compounds			
	II	III	IV	V
$(M-HCN)^+$	5,9	5,0	1,8	5,7
$(M-Hal)^+$	11,5	6,9	7,6	5,7
$(M-HalCN)^+$	1,0	0,5	0,2	0,4
$(M-HCN)-X^+$	7,9	1,0	5,2	0,8
Structure A				
$(A-CH_3)^+$	—	5,7	3,0	—
$(A-Hal)^+$	—	—	—	3,3
$(A-H)^+$	1,8	—	0,8	—
$(A-HCN)^+$	6,3	2,0	2,9	1,3
$[(A-HCN)-H]^+$	1,8	4,3	3,5	2,5
$[(M-Hal)-HNCNH]^+$	3,0	5,1	3,5	1,4
$[(M-HalCN)-HCN)]^+$	7,9	—	—	—
$[(M-HalCN)-ClC\equiv N]^+$	2,0	3,2	3,7	0,9
	49,0	52,6	35,7	21,0

*In percent of the total ion current.

An extremely important process, which is competitive with the splitting out of halogen that is usual for halo-substituted aromatic systems, is elimination of a neutral HCN particle from the molecular ion. This leads to the formation of a pseudomolecular fragment ion with a substituted imidazole structure. Splitting out of an XCN particle (X is halogen) from the molecular ion is a process with a much lower probability.

The formation of an ion that has the imidazole cation structure (structure A) with localization of the charge on the carbon atom occurs via two paths:

$$M^+ \rightarrow (M-HCN)^+ \rightarrow [(M-HCN) - \text{Halogen}]^+,$$

$$M^+ \rightarrow (M-\text{Halogen})^+ \rightarrow [(M-\text{Halogen})-HCN]^+$$

The subsequent disintegration of the ion with structure A proceeds with the loss of a neutral HCN particle; if substituent Y is a methyl group, ring expansion to give the pyrimidinium cation is possible after elimination of a hydrogen atom.

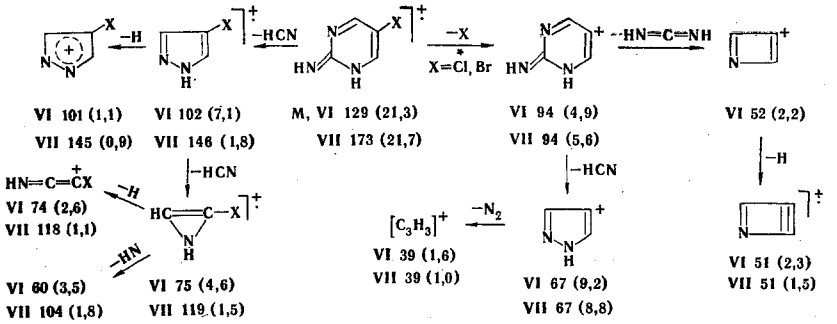
The probability of splitting out of an XCN or YCN particle (X and Y are halogens) from the molecular ion is low; the resulting four-membered ion structure is unstable and undergoes further destruction.

Disintegration of halo-substituted 2-aminopyrimidines, as in the case of 4-aminopyrimidines, is realized with destruction of the C—N bond in the molecular ion, which primarily corresponds to the imine form. In contrast to 4-aminopyrimidines, in which cleavage of the 3-4 bond prevails, the 1-2 or 2-3 bonds are cleaved here. As in the case of 4-aminopyrimidines, disintegration of the halo-substituted 2-aminopyrimidines is probably realized without the formation of ions with a conjugated diene structure, i.e., without opening of the pyrimidine ring.

It can be assumed that the loss of an HCN particle in the initial act of disintegration leads to ring contraction to a halo-substituted pyrazole structure.

Ring opening also does not occur during elimination of halogen from the molecular ion, and the positive charge, as in the case of ring-substituted aryl halides [4], is localized on the carbon atom.

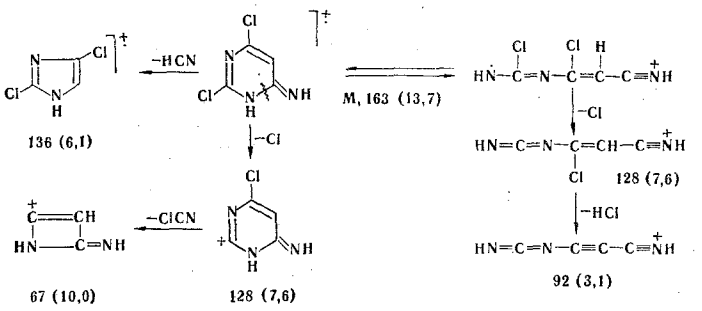
In contrast to the isomeric II (Table 2), in VI the probabilities of processes leading to the elimination of a chlorine atom or to splitting out of an HCN particle are identical. In the case of VII, as for II, the process associated with elimination of halogen predominates.



Elimination of cyanogen chloride or cyanogen bromide particles from the molecular ion, which was observed in the disintegration of II, is not realized in the mass spectra of VI and VII.

The introduction of a second halogen atom into the ring of 4-amino- or 2-aminohalo-substituted pyrimidines sharply decreases the W_M value (Table 1).

Thus the W_M values of V and VIII are, respectively, 13.7 and 12.0, while the W_M values of II, VI, and VII are 19.7, 21.9, and 21.7, respectively. This sort of decrease in W_M is not a consequence of an increase in the volume of the molecule (W_M of III is 23.0) but is associated with the large fraction of linear structures formed in the ring opening of the excited molecular ion in the first steps of the formation of fragment ions.



The linear structure of the ion with mass 128 explains the formation of the ion with mass 92. The difficulty in the interpretation of the paths of formation of this ion was noted by Nishiwaki [3] in a discussion of the mass spectrum of VIII.

The different ratios of linear and cyclic forms of the molecular ions in the mass spectra of V and VIII are possibly responsible for the different relative probability of the formation of $(M-Cl)^+$ and $(M-HCN)^+$ ions.

LITERATURE CITED

1. R. A. Khmel'nitskii, E. A. Kunina, A. B. Belikov, and Yu. P. Shvachkin, Izv. Sel'skokhoz. Akad. im. Timiryazeva, No. 2, 231 (1971).
2. T. Nishiwaki, Tetrahedron, 22, 3117 (1966).
3. T. Nishiwaki, Tetrahedron, 23, 1153 (1967).
4. F. W. McLafferty, Anal. Chem., 34, 16 (1962).