EXPERIMENTAL

The mass spectra of X and XI were recorded with an LKB-9000 mass spectrometer at ionizing voltages of 70 and 14 eV, an emission current of 20 μA, and an ion-source temperature of 250°C. The temperature of the admission system was 20-50°C.

Compounds I, III, V, VII, and VIII were synthesized by published methods [5-7], whereas II, IV, and IX-XI were obtained by acid hydrolysis of their 4-imino analogs. The deutero analog of VI was obtained by heating V in deuteromethanol. The purity of the products was monitored by chromatography on Silufol UV-254 plates [chloroform–methanol (10:1)] and elementary analysis. The melting points of the synthesized compounds were in agreement with the literature values.

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MASS SPECTROMETRY OF BIOLOGICALLY ACTIVE SUBSTANCES.

III.* MASS SPECTRA AND PECULIARITIES OF THE FRAGMENTATION OF 4-AMINO-5-PYRAZOLONES

A. I. Ermakov, V. G. Voronin, A. P. Pleshkova, Z. I. Shramova, and Z. A. Panfilova

UDC 543.51:547.775'778.2

As compared with alkyl substituents, amino and amido groups in the 4 position of 1-phenyl-2,3-dimethyl-5-pyrazolones substantially reduce the stability of the molecule with respect to electron impact. The rearrangements in the heteroring that are characteristic for alkyl-substituted pyrazolones are absent in the fragmentation of these compounds. The principal fragmentation process in this case is manifested in the primary formation of a $CH_3C{\equiv}NCH_3^+$ ion with cleavage of the ring C=C and N–N bonds. The peculiarities of the mass spectra of 4-aminopyrazolones are explained by ionization of the molecule at the C=C bond and competitive distribution of the charge in the molecular ion between the nitrogen atom of the substituent and the pyrazolone ring. The spectra at low ionizing-electron energies were studied.

The mass-spectrometric fragmentation of the simplest pyrazolone systems has been studied in detail in the case of Δ^2-pyrazolin-5-one derivatives with alkyl substituents in the 4 position [2]. Less study has been devoted to Δ^3-pyrazolin-5-one derivatives in this respect, but compounds with alkyl or acyl substituents also predominate in this series [3, 4].

In the present research we examined the mass spectra, obtained at different ionizing energies (70 and 14 eV), of a number of 1-phenyl-3-methyl-5-pyrazolones (I-VII) with nitro-

*See [1] for communication II.

Branch of the S. Ordzhonikidze All-Union Scientific-Research Pharmaceutical-Chemistry Institute, Kupavna, Moscow Oblast 142450.

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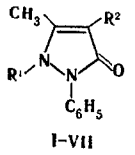
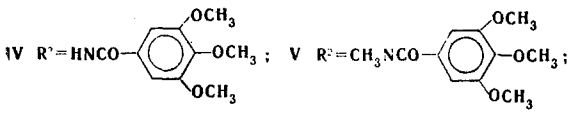
gen-containing substituents in the 4 position. The spectra of I-V were investigated for the first time in the present research.



I-VII

I-V, VII $R^1=CH_3$; I $R^2=NH_2$; II $R^2=NHCH_3$; III $R^2=N(CH_3)_2$;



IV $R^2=HNCO$; V $R^2=CH_3NCO$;

VI $R^1=R^2=H$; VII $R^2=H$

We assumed that the selection of the substituents in I-V and a study of the low-voltage spectra and the doubly charged ions would make it possible to reveal in greater detail the mechanisms of the fragmentation of the pyrazole ring than has been possible only on the basis of [1-4]. For most of the previously studied pyrazolones with alkyl and acyl substituents the fragmentation is determined primarily by the substituting groups and is accompanied by skeletal rearrangements of the heteroring.

Pyrazolones VI and VII, as well as 1-phenyl-2,3,4-trimethyl- (VIII), 1,2,3,4-tetramethyl- (IX), and 1-phenyl-3-methyl-4-amino-5-pyrazolones (X), were used as model compounds in the interpretation of the mechanisms of the fragmentation of 4-aminopyrazolones I-V. We borrowed the mass spectra of VIII-X from [1-4].

A number of regularities that radically distinguish their behavior from the behavior of the similarly constructed VII-X under electron impact are observed in the fragmentation of I-III (Table 1). First, as compared with the CH_3 substituent in VIII, the amino group substantially lowers the relative intensity of the molecular-ion peak (M^+) and the stability of the molecule with respect to electron impact (W_M = 4.0)*; this parameter is much higher (22.0) for methyl analog VIII, and the M^+ peak is the principal peak in the spectrum. Second, intense peaks of fragments with m/e 84, 83, 57, and 42, the analogs of which are completely absent in the spectra of VI-X, are observed in the spectrum of I. Third, the maximum peak for I-III corresponds to the $CH_3C{\equiv}\overset{+}{N}CH_3$ characteristic ion with m/e 56 (e), whereas this fragment is of low intensity in the spectra of the other compounds. The fragmentation of VIII proceeds primarily with intensive rearrangments in the heteroring [1].

The relative intensity of the e ion peak decreases sharply when the ionizing voltage is lowered (Table 1), and it is consequently not a rearranged ion. Cleavage of the $C_3{=}C_4$ and N–N bonds should occur for the formation of the e fragment ion.

This process can be explained from the assumption that ionization of the molecules is realized at the ring double bond to give M_1^+ (Scheme 1).

The W_M values for I-III increase in proportion to the number of methyl groups attached to the exocyclic nitrogen atom and are, respectively, 4.0 (I), 9.9 (II), and 18.3 (III). The fact that the relative intensities of the peaks of the doubly charged ions (M^{++}) in this case also increase from 0.75% (II) to 6% (III) whereas an M^{++} peak is absent in the spectrum of I is also noteworthy.

As compared with the methyl substituent, an amino group attached to the double bond increases the probability of ionization of I at the C=C bond. The low relative intensity of the M^+ peak (14%) constitutes evidence that in this case M^+ exists in open form a, and this facilitates the formation of both ion e and ion b (Scheme 1) but excludes the formation of a stable doubly-charged ionized M^{++}. The increase in the intensity of the b ion peak at 14 eV provides evidence that the $M_1^+ \rightarrow a \rightarrow b$ process has a low energy of activation or a low frequency factor. The subsequent fragmentation of ion b does not contradict the structure assigned to it and is confirmed by the metastable ions.

On passing from I to II and III the nitrogen atom of the substituent becomes more electron-saturated as compared with the C=C bond, and the molecular ions (M_2^+) (Scheme 1) of II and III are stable with respect to fragmentation because of the stabilizing positive inductive effect of the methyl groups and the absence of an ion-radical center directly in the ring. In the case of localization of the charge on the exocyclic nitrogen atom release of the surplus energy in M_2^+ is realized in the form of self-ionization through ejection of the

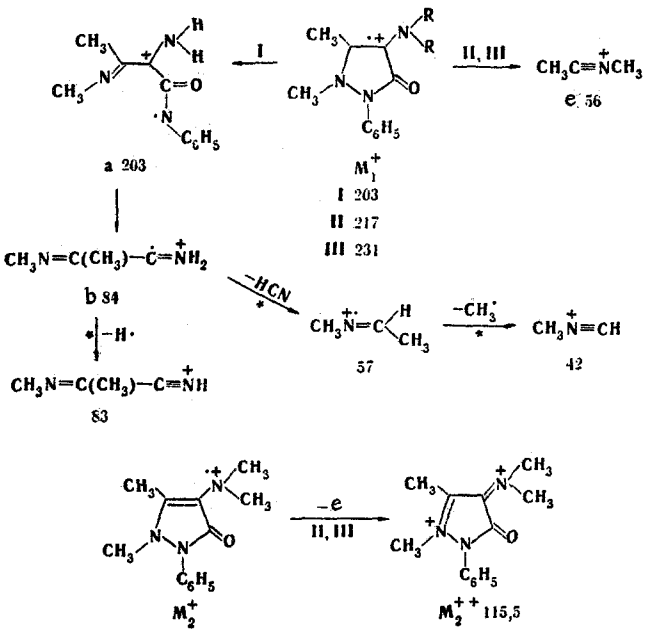
*The stability is given by the expression $W_M = I_{[M^+]}/\Sigma I$, where $I_{[M^+]}$ is the intensity of the molecular-ion peak, and ΣI is the total ion current.

TABLE 1. Mass Spectra of I-VII at 70 (a) and 14 eV (b)

Compound	m/e values (relative intensities of the ion peaks)
I[a]	39 (6), 41 (5), 42 (63), 43 (4), 51 (10), 54 (8), 55 (4), 56 (100), 57 (56), 58 (4), 77 (12), 83 (14), 84 (30), 85 (3), 91 (4), 92 (3), 93 (4), 119 (3), 147 (3), 202 (2), 203 (14), 204 (3)
I[b]	56 (25), 57 (6), 83 (20), 84 (64), 93 (6), 119 (13), 203 (100), 204 (20)
II[a]	39 (5), 40 (3), 41 (5), 42 (18), 51 (6), 54 (4), 55 (6), 56 (100), 57 (12), 77 (6), 83 (25), 84 (3), 91 (5), 92 (3), 93 (9), 98 (6), 119 (9), 123 (6), 215 (3), 216 (6), 217 (30), 218 (5)
IIb	56 (41), 83 (12), 93 (13), 98 (24), 119 (12), 123 (6), 215 (6), 216 (12), 217 (100), 218 (18)
III[a]	41 (3), 42 (10), 51 (4), 54 (3), 55 (6), 56 (100), 57 (6), 77 (10), 97 (42), 98 (3), 111 (20), 112 (10), 119 (3), 123 (8), 216 (4), 230 (10), 231 (76), 232 (12)
IIIb	56 (3), 57 (2), 97 (13), 111 (3), 112 (9), 119 (3), 216 (2), 230 (5), 231 (100), 232 (16)
IV[a]	39 (2), 41 (4), 42 (6), 43 (5), 55 (2), 56 (54), 57 (10), 77 (6), 84 (5), 85 (4), 91 (5), 92 (2), 93 (4), 109 (2), 119 (6), 137 (4), 152 (6), 167 (2), 195 (100), 196 (12), 202 (6), 203 (5), 217 (4), 381 (2), 397 (41), 398 (12),
IV[b]	56 (12), 84 (12), 119 (12), 195 (12), 203 (12), 217 (13), 397 (100), 398 (32)
V[a]	39 (2), 41 (3), 42 (4), 55 (4), 56 (68), 57 (4), 77 (8), 78 (3), 91 (4), 122 (4), 123 (18), 137 (5), 152 (6), 167 (2), 195 (100), 196 (12), 216 (64), 217 (10), 236 (4), 292 (2), 395 (4), 396 (10), 397 (3), 411 (70), 412 (18)
Vb	56 (4), 195 (18), 216 (23), 217 (6), 292 (4), 396 (4), 400 ( ), 411 (100), 412 (22)
VI[a]	39 (12), 40 (4), 41 (10), 42 (6), 43 (6), 50 (4), 51 (14), 52 (3), 63 (6), 64 (10), 65 (4), 69 (4), 77 (60), 78 (10), 91 (6), 92 (6), 96 (4), 104 (3), 105 (28), 106 (6)
VIb	132 (10), 133 (2), 145 (3), 146 (2), 174 (100), 175 (20), 105 (4), 132 (2), 174 (100), 175 (8)
VII[a]	39 (10), 40 (4), 41 (6), 42 (5), 51 (8), 55 (8), 56 (22), 57 (3), 77 (33), 78 (4), 82 (5), 84 (6), 91 (6), 92 (4), 93 (9), 96 (44), 97 (4), 105 (15), 106 (8), 129 (4), 130 (4), 145 (4), 159 (4), 173 (7), 187 (10), 188 (100), 189 (14)
VII b	84 (2), 93 (2), 96 (12), 105 (2), 187 (4), 188 (100), 189 (14)

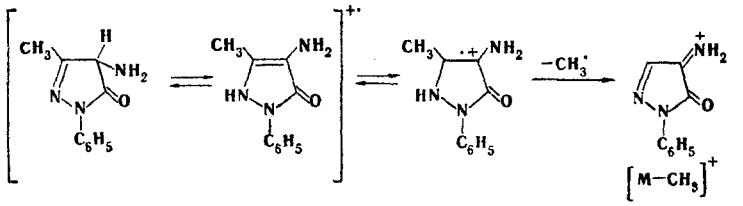
free (nonbonding) electron by the ring N_2 atom to give doubly charged M^{++} (Scheme 1), the electronic structure of which satisfies the Hückel aromaticity requirement; this is also responsible for its higher stability [5]. This reasoning does not contradict the fact that in the absence of a primary ionization center the number of methyl groups attached directly to the ring does not affect the stability of the molecules with respect to electron impact, as observed for VI-VIII: W_M = 24 (VI), 25 (VII), and 22 (VIII).

Scheme 1



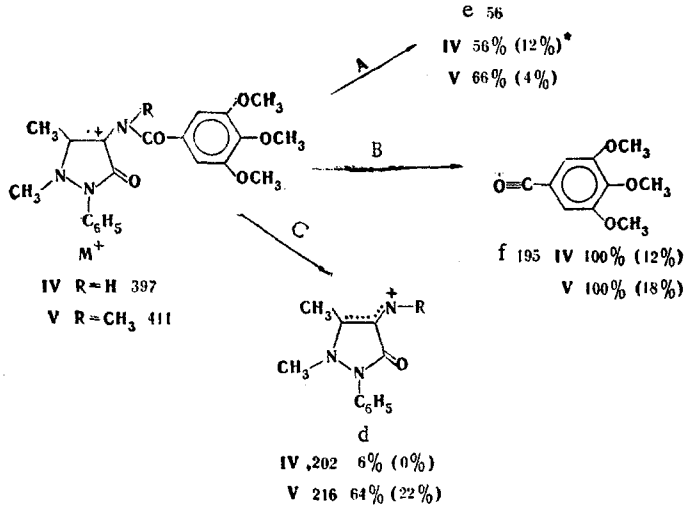
The specific character of the fragmentation of Δ^2-pyrazolin-5-one with an amino group in the 4 position (X) as compared with I-III is manifested in the intensive detachment of a CH_3 radical. This is probably not simple detachment of the substituent as assumed in [4] but rather a rearrangement reaction due to the labile hydrogen atom, tautomerism, and localization of the charge on the amino group (Scheme 2). It is not difficult to see that the $[M - CH_3]^+$ ions and the previously examined M^{++} ions have similar structures.

Scheme 2



A study of the behavior of the pyrazolone ring when several competitive fragmentation reactions are taking place seems of interest. The fragmentation of IV and V is realized via three pathways:

Scheme 3



A comparison of the intensities of the e and f ion peaks at 70 and 14 eV once again shows that the e ions are formed as a result of simple bond cleavage, since the relative intensities of the peaks of both ions change proportionally when the ionizing voltage is changed, and the formation of a trimethoxybenzoyl cation in the case of simple bond cleavage has been proved rigorously for many compounds [6]. It also follows from the mechanisms of the formation of ions e (Scheme 1) and f (Scheme 3) that pathway B is energically more favorable and that the f ion peak is the maximum peak in the spectrum. It is interesting to note that the cleavage of the amide bond in the M^+ (pathway C) is more characteristic for V and that the peak of the cyclic ion with m/e 216 in the spectrum of V at 70 and 14 eV is the second most intense peak, whereas the intensity of the analogous peak with m/e 202 in the spectrum of IV is extremely low. This is probably associated with the more effective stabilization by the methyl group of the charge on the nitrogen atom of the substituent in fragment d.

Thus as a result of a study of the 3-pyrazolinones it was established that amino and amido groups may change the character of the fragmentation of the pyrazolone ring. The principles found in this research can be used to establish the structures of related compounds by mass spectrometry.

EXPERIMENTAL

The mass spectra of the compounds were recorded with an LKB-9000 mass spectrometer at ionizing voltages of 70 and 14 eV, an emission current of 200 μA, and an ion-source tempera-

*The intensities at 14 eV are indicated in parentheses.

ture of 250°C. The temperature of admission of the compounds into the ion source was 50-70°C.

Compounds I [7], II [8], III [9], IV [10], V [13], VI [11], and VII [12] were synthesized by previously described methods.

All of the compounds were purified prior to mass-spectral analysis by recrystallization and were identified from the melting points and the results of elementary analysis.

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METHYLATION OF PYRIMIDINE DERIVATIVES

V. G. Voronin, S. B. Goncharenko, Yu. N. Portnov, A. I. Ermakov, and M. I. Shemeryankina

UDC 547.854.83

A mixture of isomers that differ with respect to the position of the methyl group is formed in the methylation of 5,5-diethyl-6-imino-5,6-dihydro[1H,3H]pyrimidine-2,4-dione with excess methyl iodide in the presence of ethoxide. Isomerization of the Dimroth-rearrangement type was observed. The mass spectra of the isomers are examined, and the IR spectra of the tautomeric forms are discussed.

Iminobarbituric acids are widely used as starting compounds in the synthesis of biologically active barbituric [1] and 4-thiobarbituric acids [2] and their N-alkyl derivatives. The alkylation of barbituric acids, which can lead to both N- and O-derivatives [3, 4], depending on the reagents used, serves as an important method for the synthesis of the latter. In the present research in the case of 5,5-diethyl-6-imino-5,6-dihydro[1H,3H]pyrimidine-2,4-dione and its N-substituted analogs we studied methylation with methyl iodide in the presence of ethoxide as the base. Under the selected conditions and at a reagent molar ratio of 1:1:1 the 3 position of I is methylated to give monomethyl derivative III (see the scheme below); this is in agreement with the high NH acidity of this position and the data in [1].

The action of two or more moles of methyl iodide and sodium ethoxide on 1 mole of pyrimidinedione I leads to the formation of a mixture of isomers IV and V in a ratio of 3:2. A similar result was obtained in the methylation of III under the same conditions, whereas II gives only 1,3-dimethyl derivative IV. This result provides evidence that the dialkylation of I includes the initial formation of monomethyl derivative III, which subsequently undergoes further alkylation. The formation of a mixture of isomers IV and V is associated with

Branch of the S. Ordzhonikidze All-Union Scientific-Research Pharmaceutical-Chemistry Institute, Kupavna, Moscow Oblast 142450.

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