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MASS-SPECTROMETRIC STUDY OF THE CYCLIZATION OF DIAZO COMPOUNDS.

9.* 2-DIAZO-2-CYANOACETAMIDES

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UDC 543.51:547.791.4

An analysis of the electron impact mass-spectra of 2-diazo-2-cyanoacetamides and the 4-cyano-5-hydroxy-1,2,3-triazoles isomeric to them, showed that the molecular ions of these compounds do not isomerize one into another. The diazo compounds decompose, undergoing a Wolff rearrangement. To study the fragmentation of the diazoamides, one can use the crystalline adducts of these diazo compounds with triphenylphosphine, and to study the fragmentation of the triazoles, their salts with aliphatic amines.

It was shown previously [2] that diazoketones with a heteroatomic grouping in the carbon chain eliminate a molecule of nitrogen and cyclize to form heterocyclic compounds. This takes place in solution by the action of an acid as well as in the gas phase by the action of electron impact. Such an analogy allowed a prediction to be made on the basis of mass-spectral data of the direction and approximate yield of the cyclic product when the reaction was carried out in solution [1, 2].

The question of th linear or cyclic form of diazo compounds containing C=O, C=S, or C=NH groups in position α to the diazo group has already been investigated in papers by Wolff [3, 4] and Dimroth [5]. At the present time, it is reliably known that diazoketones and diazoesters exist exclusively in the linear form [6]: the alternative, 1,2,3-oxadiazole form is unstable and is easily opened as a result of an electrocyclic reaction to the more stable linear form [7]. Diazothioketones exist exclusively in the form of thiadiazoles and attempts to obtain these compounds in the linear form have not, so far, led to success [6]. Diazoamides occupy an intermediate position and can exist in the linear form as well as in the cyclic, triazole form, which can, under certain conditions, change back and forth [6, 8, 9]. These structural features of diazo compounds are determined unambiguously by the increase in the electronegativity of the heteroatoms in the order S < N < O.

Comparing the stability of the molecular ions (M^+) of the linear diazo compounds and their isomeric heterocyclic systems, one can suppose that M^+ of the cyclic isomers should be rather stable (aromatic system) and decompose along a specific path characteristic for such ring. At the same time, M^+ of the linear, diazo compounds are significantly less stable, as a rule, and in the spectra of many of them, the M^+ peak is not observed at all [1, 2, 9].

*See [1] for No. 8 in the series.

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TABLE 1. Intensities of the Peaks Characterizing the Ionic Fragments in the Mass-Spectra of Compounds I-IV

Compound	m/z, intensity (in %) of the ionic peaks													
	110	82	81	67	66	64	58	54	53	52	44	43	39	38
I	27,3	10,5	—	7,7	1,9	<0,1	—	5,8	2,6	9,1	0,9	14,5	4,5	8,9
II	53,2	1,1	1,5	2,3	0,4	1,4	4,9	0,9	1,7	17,8	2,1	1,3	1,5	3,2
III	27,5	14,3	—	5,9	2,0	<0,1	—	4,1	2,1	6,5	0,8	11,4	5,7	7,3
IV	54,0	0,9	1,6	2,3	0,3	0,5	4,8	0,8	1,6	19,0	2,2	1,4	1,4	3,2
V	50,1	0,9	1,5	1,9	0,3	0,5	6,6	0,7	1,7	19,3	2,1	1,3	1,4	3,5

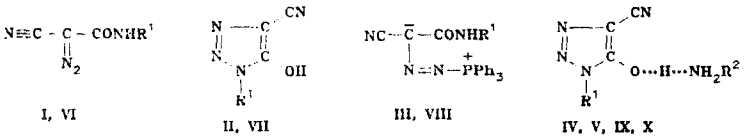
TABLE 2. Elemental Composition of Some Ionic Fragments of Compounds I-V from High-Resolution Mass-Spectrometry

Ion mass	Composition	Found (compound)	Calculated
44	$CONH_2$	44,0143 (I), 44,0145 (IV)	44,0136
54	C_2NO	53,9989 (I), 53,9984 (II)	53,9979
	$C_2H_2N_2$	54,0202 (I), 54,0197 (II)	54,0186
55	C_2HNO	55,0042 (I), 55,0051 (II)	55,0057
58	CN_2H_2O	58,0167 (II)	58,0162
64	C_3N_2	64,0090 (II), 64,0086 (V)	64,0092
67	C_3HNO	67,0069 (I), 67,0059 (II)	67,0057
	C_2HN_3	67,0181 (I), 67,0169 (II), 67,0178 (III)	67,0171

In the case of the diazoamides and their isomeric triazolates, this position has experimental support [9].

In studying the decomposition of diazoesters, the authors of [10] came to the conclusion that the high stability of the M^+ ions of these compounds, which was noted earlier in [11], was apparently to be explained by the isomerization of M^+ to heterocyclic systems and especially to oxadiazoles. In their opinion, the excess energy of M^+ (a range of 0-20 eV [12]) allows the linear form to isomerize to the cyclic, although this does not occur in solution at the low energies common to thermal excitation [3-7]. Possibly, this process is also explained by the low electron density on the diazo group in the M^+, inasmuch as the charge in the M^+ of diazo compounds is localized on the diazo group itself [13]. Thus, the formation of the cyclic form of diazoesters as a result of electron impact is quite realistic; i.e., even so electronegative an element as oxygen can form a bond to a diazo group. Consequently, it was proper to expect that the cyclization of the M^+ of diazoamides to triazoles would take place more readily when the alkoxy group was replaced by an amino group, inasmuch as a nitrogen atom is less electronegative and bonds to a diazo group more readily than an oxygen atom [6].

In studying the possible isomerization of diazoamide M^+ to triazoles, we analyzed the mass-spectra of compounds I-X. It must be noted that in solution, diazoamides I and VI are converted by the action of bases into triazolates IV, V, IX, and X, which, on acidification of the solution, change into triazoles II and VII [14].



I—V R^1=H; VI—X R^1=CH_3; IV, IX R^2=H; V, X R^2=CH_3

As can be seen from Table 1, the differences in the relative intensities of the peaks of the ionic fragments in the spectra of diazoamide I and its crystalline adduct with triphenylphosphine, III, are insignificant. This allows one to use adduct III, which is easily isolated from the reaction medium, to study the behavior of the less readily accessible diazoamide I under the action of electron impact. There is also almost complete agreement

TABLE 3. Intensities of the Peaks Characterizing the Ionic Fragments in the Mass-Spectra of Compounds VI-X

Compound	m/z, intensity (in %) of the ionic peaks												
	124	96	95	81	69	68	67	66	58	54	53	39	38
VI	18,5	12,4	—	3,2	4,5	1,7	6,1	1,6	13,1	6,0	9,8	2,9	4,4
VII	25,4	0,9	1,1	3,5	0,9	3,4	15,9	0,7	4,3	3,5	21,2	2,0	3,0
VIII	18,3	11,1	—	5,2	5,0	1,5	4,7	2,0	10,0	5,3	8,6	5,4	5,4
IX	22,7	0,6	1,1	3,5	0,8	3,4	15,8	0,7	4,2	3,7	21,4	2,0	3,1
X	24,8	2,0	1,0	3,6	1,2	3,0	15,0	0,7	5,1	4,0	21,0	2,0	3,2

TABLE 4. Elemental Composition of Ions of Compounds VI-X from High-Resolution Mass-Spectrometry

Ion mass	Composition	Found (compound)	Calculated
53	C_2N_2H	53,0152 (VI), 53,0146 (IX)	53,0140
67*	C_3HNO	67,0060 (VI), 67,0054 (IX)	67,0058
	C_2HN_3	67,0174 (VI), 67,0182 (IX)	67,0171
	$C_3H_3N_2$	67,0301 (VI), 67,0308 (VII), 67,0302 (IX)	67,0296
68**	C_3H_2NO	68,0124 (VI), 68,0131 (IX), 68,0129 (X)	68,0136
	$C_3H_4N_2$	68,0365 (VI), 68,0380 (IX), 68,0371 (X)	68,0376
69	C_3H_3NO	69,0204 (VI), 69,0207 (VII)	68,0214
81	C_3N_2HO	81,0085 (VI), 81,0084 (IX)	81,0089

*The ratio of the intensities of the peak of ions C_3HNO:C_2HN_3: $C_3H_3N_2$ in the spectrum of diazoamide VI is 3:5:2, and 2:5:100 in the spectrum of triazole IX.

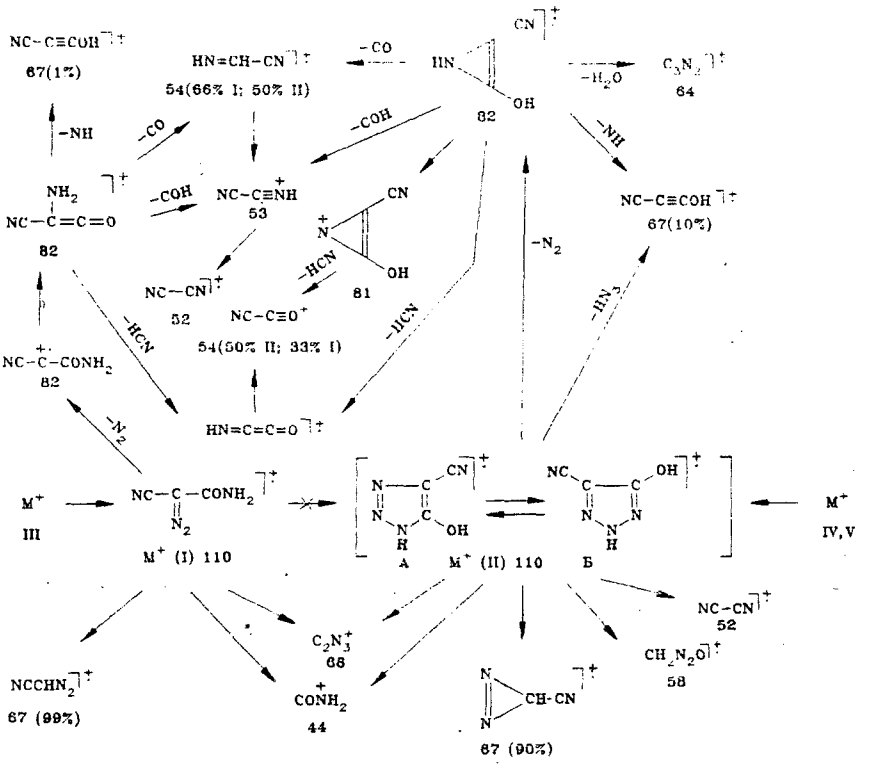
**The ratio of the intensities of the peaks of ions C_3H_2NO: $C_3H_4N_2$ in the spectrum of diazoamide VI is 1:4, and 1:3 in the spectra of triazoles IX and X.

between the spectra of triazole II and triazolates IV and V; i.e., M^+ of the latter lose a molecule of amine and form a pseudomolecular triazole ion. It must be noted that it is the triazole ion itself that is formed, not the supercharged triazolate anion, as observed in [9]. This is explained by the lower acidity of the triazoles studied and the consequent lower ionicity of the bond between the heterocycle and the amine. Such a conclusion regarding the structure of triazolates IV and V is in complete agreement with the data from NMR spectroscopy [14]. Thus, it is possible to use triazolates IV and V to study the decomposition of triazole II.

Along with this, it can be seen from Table 1 that the mass-spectra of diazoamide I and its isomeric triazole II differ substantially, supplying grounds for the conclusion that the M^+ of these compounds differ structurally. Analysis of the mass-spectra and of the data in [15, 16], allowed us to describe the decomposition of cyclic triazoles by the scheme given below. The fragmentation of the diazoamide M^+ starts with the elimination of a molecule of nitrogen accompanied by a Wolff rearrangement [17, 18], although in this case it is an amino group, not an alkyl radical that migrates. Another characteristic path is the rupture of the $C(N_2)$—CO bond (see Scheme 1) with the formation of ions 44 and 66.

As can be seen from Table 1, the maximum ion in the spectra of compounds I-V is M^+ with a mass of 110, while its intensity in the case of the linear diazoamide is about one-half, which was also to be expected. Moreover, the $[M - N_2]^+$ ion (82) is also observed for both isomers, the intensity being 10 times greater in the case of the linear form, in complete accord with the data on the decomposition of diazo compounds [1, 2, 17, 18]. The formation of ion $[M - N_2, -H]^+$ (81) is possible only from the cyclic form, the triazole [15, 16], while this process is not characteristic of the linear ion (82) forming through the decomposition of the diazoamide. The total lack of the peak for this ion with compounds I and III is evidence that the isomerization of the linear 110 ion to a cyclic form does not take place. This is also shown by the absence of peaks of ions 58 and 64 in the spectra of diazoamides I and III (see Table 1). The first of them is formed by splitting out cyanogen from the B tautomeric form of the triazole [15], and the second, by splitting out a water molecule from

Scheme 1



cyclic ion 82. The existence of part of M^+ of triazole II in the form of tautomeric form B is supported by the formation of ions 52 and 67, besides ion 58. The peaks of the two former are quite intense. Besides the $[M - N_2]^+$ ion, the formation of ions with masses 67, 66, 44, and 38 are characteristic of the linear structure (see Scheme 1 and Table 1).

The elemental composition of several ions was confirmed by means of high-resolution mass-spectrometry (Table 2).

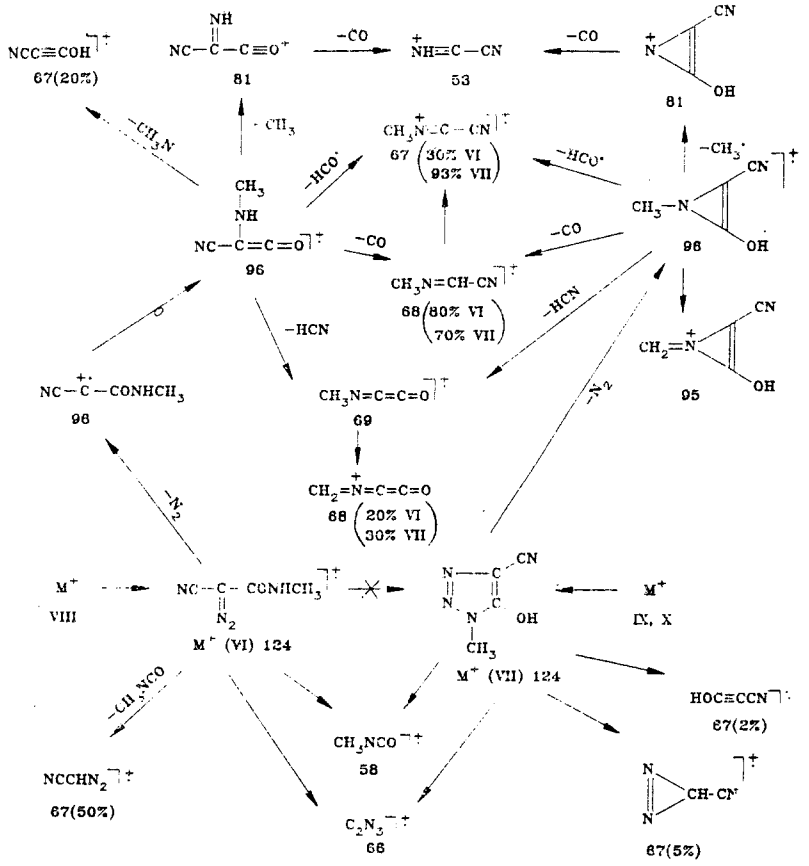
Ions 54 and 67 are compound. The ratio of intensities of the peaks of ions $C_2NO/C_2H_2N_2$ in the mass spectra of compounds II, IV, and V is 1:1, whereas for compounds I and III it is

TABLE 5. Mass-Spectra of Compounds I-XI

Compound	Values of m/z (relative intensities of the peaks of the ions in percent of the maximum)*
I	110 (100); 82 (38,4); 67 (28,6); 55 (21,9), 54 (10,7); 53 (34,2); 44 (54,8); 43 (12,8); 39 (17,5); 38 (34,2)
II	111 (5,1); 110 (100); 67 (3,9); 64 (4,5); 58 (9,0); 54 (3,9); 53 (34,5); 52 (4,2); 39 (4,8); 38 (6,3)
III	110 (100); 82 (46,1); 67 (18,5); 55 (15,4); 54 (7,7); 53 (24,6); 44 (43,0); 43 (13,8); 39 (21,5); 38 (27,7)
IV	111 (5,1); 110 (100); 81 (3,2); 67 (4,4); 58 (9,2); 54 (3,4); 53 (36,9); 52 (4,3); 43 (4,0); 38 (6,2)
V	111 (5,1); 110 (100); 81 (3,1); 67 (3,8); 58 (14,1); 54 (3,9); 53 (39,9); 52 (4,2); 43 (4,4); 38 (7,3)
VI	124 (100); 96 (69,2); 81 (17,6); 69 (25,3); 67 (34,4); 58 (72,4); 54 (34,4); 53 (55,2); 39 (16,3); 38 (24,9)
VII	124 (100); 81 (13,8); 68 (13,4); 67 (62,6); 58 (16,9); 54 (13,8); 53 (83,5); 41 (12,7); 39 (7,9); 38 (11,8)
VIII	124 (100), 96 (61,6); 81 (28,0); 69 (27,7); 67 (26,1); 58 (55,6); 54 (29,4); 53 (47,8); 39 (30,0); 38 (30,0)
IX	124 (100); 81 (15,6); 68 (16,0); 67 (70,4); 58 (18,4); 54 (17,4); 53 (97,2); 41 (12,8); 39 (9,2); 38 (14,0)
X	124 (100); 96 (9,6); 81 (14,7); 68 (12,5); 67 (59,7); 58 (20,7); 53 (83,3); 41 (12,7); 39 (8,2); 38 (13,1)
XI	138 (100); 95 (50,0); 81 (41,7); 72 (70,8); 69 (87,5); 67 (79,2); 44 (37,5); 42 (66,7); 39 (16,5); 38 (20,4)

*The ten strongest peaks in the spectrum are given.

Scheme 2



1:2. This agrees with the easy decomposition of the ketones forming as a result of the Wolff rearrangement with the elimination of a molecule of CO [17, 18]. The ratio of the intensities of the peaks of ions C_3HNO/C_2HN_3 (67) on the decomposition of the cyclic structures is 1:10, but 1:100 for the linear ones. This fact is explained by the impossibility of splitting out an HN_3 molecule in a single step in the case of the diazoamide and the disadvantage in splitting out an NH particle from an $[M - N_2]^+$ ion. Both paths are possible for the triazole, although as the low intensities of these fragments show, neither are very effective in this case as well.

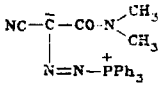
Substitution of a methyl on the nitrogen atom introduces a substantial change in the mechanism of the decomposition of the compounds being studied that allows one to suggest a specific scheme for the decomposition of compounds VI-X based on data from the ordinary spectra and high-resolution spectra (Tables 3 and 4).

The spectra of compounds VI and VIII, as of VII, IX, and X, are consistent among themselves; i.e., the conclusion drawn from the analysis of the spectra of compounds I-V concerning the possibility of studying the behavior of diazoamides under the action of electron impact from the spectra of their triphenylphosphine adducts and of studying the behavior of the triazoles from the spectra of the triazolates is completely confirmed. At the same time, the differences in the relative intensities of the fragment ions formed during the decomposition of the linear (VI, VIII) and cyclic (VII, IX, X) compounds are sufficiently great so that one can conclude that in this case the isomerization of M^+ of diazoamide VI to the M^+ of triazole VII does not take place; i.e., the structure of the M^+ of these compounds is different.

A methyl substituent on the nitrogen atom precludes the tautomeric conversion to the triazole and leads not only to a decrease in the stability of M^+ but also the impossibility of decomposition by elimination of a cyanogen molecule (ion 72, analogous to ion 58 for compounds II, IV, and V, is completely absent for compounds VII, IX, and X). It also decreases the fraction of $[M - CH_3NCO]^+$ ion in the total current of isobaric ions of mass 67 (see Table 4) from 90 to 5%. The $[M - N_2, -H]^+$ ion (95) peak, which is characteristic of the decomposi-

tion of triazoles, is completely absent for diazoamides VI and VIII, showing that these compounds do not isomerize to the M^+ of the triazoles. The decomposition of the linear diazo compounds without cyclization is confirmed by the high intensities of the $[M - N_2]^+$ ions (96) and ions 69 and 58. Ions 67 and 53, the peaks of which are very intense (see Table 3), are most characteristic of the decomposition of the cyclic structure of triazole VII. The conclusion drawn concerning the different structures of M^+ in the case of triazole VII and diazoamide VI is also confirmed by the high-resolution spectra (see Table 4). The increase in the fraction of the $C_3H_4N_2$ ion current with respect to that of the isobaric C_3H_2NO ion in the decomposition of diazoamide VII is explained by the elimination of CO, which is characteristic of ketones and was noted in the discussion of the decomposition of compounds I-V. Splitting out a molecule of CH_3NCO from the linear ion is considerably more advantageous than from the cyclic M^+ where the tautomeric conversion is impossible. On the other hand, elimination of an HCO radical from the cyclic $[M - N_2]^+$ ion occurs readily. This explains the differences in the relative intensities of the isobaric ions with mass 67 (see Table 4).

To verify the mechanism of decomposition of diazoamides, we synthesized the dimethyl substituted compound, which is unable to cyclize in solution.



XI

The adduct of this compound with triphenylphosphine, XI, was studied mass-spectroscopically. All of the peaks observed in its spectrum (Table 5) are produced by ions forming as a result of the Wolff rearrangement or of the rupture of single bonds in the linear $[M - PPh_3]^+$ ion (138).

Thus, analysis of the mass-spectra of compounds I-XI has shown that the isomerization of M^+ of diazoamides to M^+ of triazoles is not observed. Differences in the behavior of the investigated diazoamides under electron impact and in solution [14] are apparently explained by the fact that the first step in the isomerization in solution is the splitting out of a proton to form an anion capable of isomerizing while in the gas phase a cation-radical undergoes transformation. The possibility of finding an isomerization product in the gas phase with the help of mass-spectrometry of negative ions is not precluded. The elucidation of this matter is the goal of future investigations.

EXPERIMENTAL

Compounds I-XI were all obtained by the procedure in [14]. The mass-spectra were taken on an MAT-311 A instrument with use of a system for the direct introduction of a sample into the ion source at a temperature of 20°C. It should be noted that when the samples were heated, the intensity of the M^+ peak decreased sharply with a simultaneous increase in the intensities of fragments with masses of 44 and 53 (I-V), 53 and 58 (VI-X), and 68 and 72 (XI). At temperatures of 110-130°C, the mass-spectra of the cyclic and linear compounds become identical because the same products are formed as a result of thermal decomposition and further ionization of these leads to analogous mass-spectra. It is exactly to avoid thermal decomposition that the spectra of compounds I-XI are obtained without heating the inlet. Electron energy, 75 eV.

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SYNTHESIS AND CONVERSIONS OF 2-ARYL DERIVATIVES OF s-TRIAZOLO[4,3-a]PYRIMIDINE

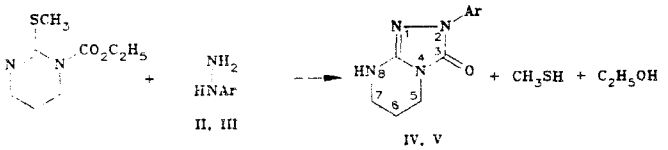
I. Krezhel'

UDC 547.853'792'556.8.07: 543.422.25

The reaction of arylhydrazines and 1-ethoxycarbonyl-2-methylthio-1,4,5,6-tetrahydropyrimidines forms 2-aryl-3-oxo-2,3,5,6,7,8-hexahydro-s-triazolo[4,3-a]pyrimidines. The reaction of 2-phenyl substituted triazolo[4,3-a]pyrimidine with various acylating agents to give 8-acyl derivatives and the effect thereon of hydrogen chloride were studied. The amine-imine tautomerism of these compounds was studied by PMR spectroscopy.

Among guanidine derivatives there are substances that have a wide spectrum of pharmacological activities [1, 2]. We have previously synthesized derivatives containing guanidine residues [3] and isothioureide residues bioisosteric with guanidines [4, 5]. In a further search for new biologically active compounds, the present work undertakes to synthesize compounds containing a guanidine grouping in a cyclic system.

The starting material was 1-ethoxycarbonyl-2-methylthio-1,4,5,6-tetrahydropyrimidine (I) [6]. The reaction of compound I with phenyl- or 4-sulfonamidophenylhydrazines (II, III) forms materials of cyclic structure; on the basis of elemental analysis and IR and PMR spectra these were assigned the structures of 2-aryl-3-oxo-2,3,5,6,7,8-hexahydro-s-triazolo[4,3-a]pyrimidines (IV, V).



II, IV Ar = C_6H_5; III, V Ar = p-$C_6H_4SO_2NH_2$

When compared with the spectrum of I, the IR spectra of crystalline IV and V are characterized by the disappearance of the valence vibration band of the ether bond (1730 and 1130 cm^{-1}), and the appearance of valence and deformation vibration bands of the NH group in the 3300-3100, 1510, and 1535 cm^{-1} regions and of the amide C=O valence vibration bands in the 1690-1720 cm^{-1} region. The PMR spectra of IV and V also show the disappearance of the SCH_3 and OCH_2CH_3 proton signals and the appearance of aryl proton and NH proton signals. In connection with the presence of the amide group, these compounds can exist in the tautomeric forms A and B.

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