MASS-SPECTROMETRIC STUDY OF AZIDO-TETRAZOLE TAUTOMERISM IN THE PYRIMIDO-as-TRIAZINE SERIES

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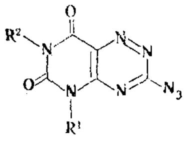
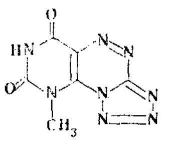
The problem of the utilization of a series of mass-spectrometric experimental data [the stabilities with respect to electron impact, the ratios of the intensities of the peaks of the ions responsible for the observed tautomerism, the first ionization potentials (FIP), the appearance potentials (AP), and the ΔE values] to distinguish the tautomeric forms in the azides and tetrazoles of pyrimido-as-triazines is discussed.

The interest in pyrimido[4,5-e][1,2,4]triazine-6,8-dione derivatives is dictated primarily by the fact that they are structural analogs of the natural antitumorigenic antibodies fervenulin, xanthothricin, and rheumycin [1].

The synthesis and properties of I-VII are described in [2, 3]. The choice between the azide and tetrazole† structures for crystalline I-VII was made from the presence or absence in the IR spectra of the characteristic absorption of the azide group and the absorption of the tetrazole ring (absorption at 2100-2200 cm^{-1} for the azide group and at 970-1000 cm^{-1} for the tetrazole ring).

In the present research we studied the possibility of the application of mass spectrometry to a study of azido-tetrazole tautomerism in the azides and tetrazoles of pyrimido [4,5-e][1,2,4]triazine-6,8-diones I-V, in an analog, viz., pyrimido[5,4-e][1,2,4]triazine-6,8-dione VI, and in VII with an open uracil ring.


I-III, V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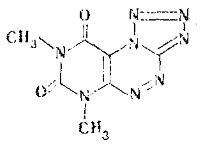
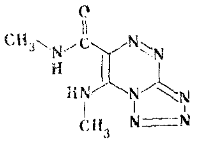

VI


VII

I $R^1 = R^2 = H$; II $R^1 = CH_3$, $R^2 = H$; III $R^1 = H$, $R^2 = CH_3$; V $R^1 = R^2 = CH_3$

If the crystalline substance exists in several isomeric (tautomeric) forms, each of them will be recorded in the form of M^+ ions that retain the topology of the structure of each isomer. The observed difference in the mass spectra in the initial stages of the fragmentation of the M^+ ions for each isomer (tautomer) follows from this.

In the present research during a study of the mass spectra of I-V we observed that splitting out of a particle with a mass of 28 amu occurs in the first stage of the fragmentation, regardless of the form of M^+ (azide or tetrazole) (Table 1). Two pathways of fragmentation of the M^+ with splitting out of 28 amu are possible for the compounds under consideration; these pathways are ejection of CO from the uracil part of the molecule or elimination of N_2. A study of the high-resolution mass spectra (HRMS) showed that splitting out of N_2, which is evidently realized from the azide or tetrazole part of the molecule rather than from the triazole ring, since in this case the energy of activation (ΔE) of the process $M^+ \xrightarrow{-N_2} [M-N_2]^+$ is lower by a factor of two to four (Table 1) than in the

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*Deceased.

†An angular structure for tetrazoles IV, VI, and VII was adopted tentatively in analogy with [4].

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TABLE 1. Stabilities of the Molecules with Respect to Electron Impact (W_M), Temperature Dependence of the Ratios of the Intensities of the Ion Peaks $I_{M^+}/I_{[M-N_2]^+}$ = A, and Photoionization Data*

Compound	W_M (m/z)	$I_{M^+}/I_{[M-N_2]^+}$				Structure of the isomer accd. to IR data	FIP, eV	AP, eV, $[M-N_2]^+$	ΔE, eV (kcal/mole)
		70°	140°	210°	280°				
I	4,1 (206)	0,40	0,37	0,39	0,35	Azide	9,20	9,28	0,08 (1,84)
II	4,5 (220)	0,80	0,85	0,82	0,86	Azide	9,24	9,48	0,24 (5,53)
III	5,3 (220)	0,52	0,60	0,61	0,55	Azide	9,35	9,54	0,19 (3,46)
IV	9,6 (220)	2,42	2,04	2,31	2,10	Tetrazole	9,11	9,35	0,24 (5,53)
V	3,8 (234)	1,23	1,26	1,42	1,33	Azide	9,06	9,49	0,33 (9,91)
VI	8,1 (234)	27,83	29,30	30,21	28,12	Tetrazole	8,80	—	—
VII†	8,6 (208)	1,23	1,30	1,28	1,20	Tetrazole	AP 8,49 $[M-NCH_3]^+$	9,66 $[M-NCH_3, -N_2]^+$	1,17 (26,97)
1-Phenyl-5-methyltetrazole						Tetrazole	8,85	9,51	0,66 (15,21)

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*Abbreviations: FIP is the first ionization potential (adiabatic), and AP is the appearance potential of the $[M-N_2]^+$ ions.

†For VII we measured the $I_{[M-NCH_3]^+}/I_{[M-NCH_3, -N_2]^+}$ = B ratio.

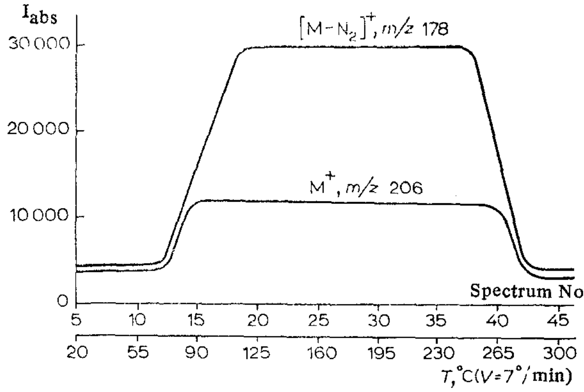

Fig. 1. Change in the absolute intensities of the M^+ and $[M-N_2]^+$ ion peaks in the mass spectrum of I.

case of elimination of N_2 from the triazine ring [5], occurs in the case of I-V.

Virtually no splitting out of an N_2 particle from M^+ is observed for VI, which retains the skeleton of the fervenulin molecule [5], and this automatically excludes the possibility of the use of mass spectrometry to determine the form of the tautomer but proves the possibility of the use of the method to distinguish the mode of annelation of the rings in a specific case. In the case of VII the splitting out process is secondary after elimination of an NCH_3 particle from M^+.

Thus, if the structure of M^+ corresponds to the structure of the molecule in the crystalline state, we should observe definite qualitative changes in the initial fragmentation processes for each tautomer, in this case in the formation of the $[M-N_2]^+$ ion for I-V or in the formation of the $[M-NCH_3, -N_2]^+$ ion for VII [6-8]. In this case the absence of rearrangement processes both in M^+ itself and in the fragment ions responsible for a certain tautomeric form from the moment of its formation up to the moment of recording (an ion lifetime of $1 \cdot 10^{-7}$ sec) should be guaranteed.

We assume that the constancy with time of the intensity ratios

$$I_{M^+}/I_{[M-N_2]^+} = A \text{ and } I_{[M-NCH_3]^+}/I_{[M-NCH_3, -N_2]^+} = B,$$

which is only slightly dependent on the vaporization temperature of the substance (Fig. 1), is sufficient for the accurate evaluation of the tautomeric form in I-V and VII, respectively. If this were not so, changes in the form of the curve in Fig. 1 and in the values of the indicated ratios would be observed.

It was demonstrated experimentally (Table 1) that the A ratio remains virtually unchanged over a rather wide temperature range. It is apparent from the data in Table 1 that $A < 1.3-1.4$ for the azide isomers. The tetrazole isomers are characterized by $A > 1.4$. Tetrazole VII, for which the elimination of N_2 is the second act in the fragmentation process, constitutes an exception. The large A value for VI is due to the very low intensity of the $[M - N_2]^+$ ion in its mass spectrum.

As expected, higher stabilities with respect to electron impact (W_M) were observed for tetrazoles IV, VI, and VII. Azides I-III and V had W_M values that were lower by a factor of approximately two. Thus the W_M values in the I-VII series can serve as a criterion in evaluating the tautomeric form.

The photoionization data also make it possible to evaluate the form of the tautomer. The first ionization potentials (FIP) of the tetrazoles are generally appreciably lower than those of azides I-III and V (Table 1). A model sample with the 1-phenyl-5-methyltetrazole structure has an AP in the same range as the AP for IV, VI, and VII. The ΔE values found for the $M^+ \xrightarrow{-N_2} [M-N_2]^+$ also differ for the azide and tetrazole forms of I-VII. It should be noted that a definite regularity in the change in the ΔE values is followed for I-V, which can exist in the form of equilibrium mixtures of tautomers in solutions. These compounds have $\Delta E < 10$ kcal/mole, while tetrazole VII and 1-phenyl-5-methyltetrazole, which do not undergo ring opening to give azides in solutions, have $\Delta E > 15$ kcal/mole.

EXPERIMENTAL

The low- and high-resolution mass spectra were obtained with a Varian MAT-311A spectrometer at an accelerating voltage of 3 kV, a cathode emission current of 1000 μA, and an ionizing voltage of 70 eV. The FIP and AP were measured with an MS-1302 mass spectrometer with a photoionization source; a hydrogen lamp was used as the source of ionizing photons. The device was equipped with a vacuum monochromator with a system for different evacuation. The resolving power of the device was 1.5-2.0 Å at half the height of the line in the spectrum. The studies were made at 600-4000 Å. The spectral range of the light source was 850 to 2000 Å. The FIP and AA were determined and calculated from the threshold value on the photoionization efficiency curve [9]. The accuracy of the determination in both cases was ±0.03 eV.

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