MASS SPECTROMETRY OF NITROGEN HETEROCYCLES.

3.* THERMAL INTRAMOLECULAR CYCLIZATION OF 2-AZOLYLAMINOPYRIDINES

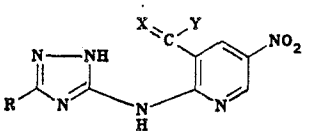
V. L. Rusinov, N. A. Klyuev, V. G. Baklykov, T. L. Pilicheva, and A. A. Tumashov

UDC 543.51'547.822.7.04

Mass spectrometric fragmentation or decay of 2-azolylaminopyridines containing a carbonyl group in the ortho-position results in elimination of a neutral molecule (ammonia, ethanol, hydrogen sulfide). This decay process is accompanied by intramolecular cyclization to form an ion with a triazolo[1,5-a]pyrido[2,3-d]pyrimidine structure.

It has previously been established that mass spectrometric fragmentation processes which involve loss of a neutral particle species in the first decomposition step infer analogous reaction pathways for thermolysis and/or photolysis reactions, or else reflect a rearrangement process in the ion [2]. These types of conversions have been observed, for example, in 1,5-disubstituted tetrazoles [3] and methyl aryl ketazines [4-6] in the occurrence of retrodiene decomposition [7, 8] and many other reactions [9].

In the present communication we have examined the behavior of previously synthesized triazolylaminopyridine derivatives [10-12] having the general structure Ia-f, under electron impact mass spectroscopic (EI-MS) acquisition conditions.



Ia-f

I a R=H, X=O, Y=NH_2; b R=CH_3, X=O, Y=NH_2; c R=H, X=O, Y=OC_2H_5; d R=CH_3, X=O, Y=OC_2H_5; e R=H, X=NH, Y=SH; f R=CH_3, X=NH, Y=SH

The structures of compounds Ia-f were established based on their PMR and ^{13}C-NMR spectral data and were confirmed by x-ray structural analysis [11]. Our mass spectrometric results are also consistent with the proposed structures. The mass spectra of compounds Ia-f contain molecular ion peaks (M^+), and their accurate masses have been determined (Table 1). In addition to their M^+ peaks ion peaks (often at maximum intensity) were detected corresponding to elimination of neutral molecules HY from the molecular ions M^+ in compounds Ia-f, where HY is ammonia, ethanol, or hydrogen sulfide (Table 1).

Analogous processes involving elimination of a hydrogen molecule have been observed in the EI-MS of diphenylamines, diphenyl ether, and its thio analog. Dehydrogenation led in these cases to the formation of a carbazole-type heterocyclic system [13]; in the diphenylamine example, the spatial or steric proximity of the phenyl nuclei guarantees that the formation of a carbazole ion (m/e 167) and the synthesis of carbazole upon heating occur relatively easily [13]. A similar process cannot be occurring during EI-MS acquisition of compounds Ia-f, since the ortho-position relative to the amino group in the pyridine ring does not contain a hydrogen atom; elimination of a neutral molecule HY from M^+ in these compounds therefore occurs via loss of a hydrogen atom from the triazole ring (from atom $N_{(1)}$) and a substituent Y in the pyridine portion of compounds Ia-f.

*For Communication 2, see [1].

S. M. Kirov Ural Polytechnical Institute, Sverdlovsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 101-104, January, 1991. Original article submitted June 5, 1989.

0009-3122/91/2701-0084$12.50

TABLE 1. Mass Spectra and HRMA Data for Compounds Ia-f

Compound	$[M]^+$ (I, %)	HRMS determined	HRMS calculated	HRMS ion molecular formula	$[M-HY]^+$ (I, %)	HRMS determined	HRMS calculated	HRMS ion molecular formula	Rest of the spectrum, m/e (I, %)
Ia	249 (33,4)	249,0612	249,0610	$C_8H_7N_7O_3$	232 (100)	232,0345	232,0345	$C_8H_4N_6O_3$	233 (16), 202 (11), 186 (23), 159 (14), 158 (8), 150 (8), 119 (8), 104 (7), 77 (15), 76 (18)
Ib	263 (62,8)	263,0768	263,0767	$C_9H_9N_7O_3$	246 (100)	246,0501	246,0501	$C_9H_6N_6O_3$	247 (16), 216 (10), 200 (33), 188 (10), 173 (13), 149 (11), 119 (12), 104 (13), 103 (15), 77 (18), 76 (23)
Ic	278 (100)	278,0759	278,0764	$C_{10}H_{10}N_6O_4$	232 (42,5)	232,0344	232,0345	$C_8H_4N_6O_3$	233 (18), 206 (81), 205 (45), 187 (14), 186 (26), 174 (12), 159 (24), 160 (12), 148 (11), 124 (13), 119 (15), 78 (11), 77 (20), 76 (15)
Id	292 (100)	292,0923	292,0920	$C_{11}H_{12}N_6O_4$	246 (53,4)	246,0502	246,0501	$C_9H_6N_6O_3$	247 (11), 220 (61), 219 (31), 200 (14), 194 (11), 173 (15), 148 (16), 124 (15), 119 (19), 77 (16), 76 (12)
Ie	265 (25,5)	265,0385	265,0382	$C_8H_7N_7O_2S$	231 (32,3)	231,0504	231,0505	$C_8H_5N_7O_2$	263 (100), 217 (29), 185 (13), 175 (10), 149 (10), 135 (11), 103 (12), 84 (27), 76 (16)
If	279 (20,6)	279,0533	279,0538	$C_9H_9N_7O_2S$	245 (100)	245,0665	245,0661	$C_9H_7N_7O_2$	246 (15), 215 (4), 199 (25), 191 (5), 172 (5), 149 (12), 103 (17), 102 (9), 83 (6), 76 (17)

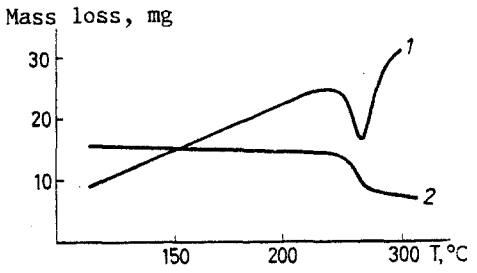
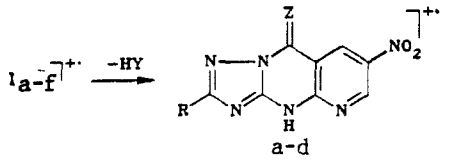


Fig. 1. Results of a thermostability study of compound Ib: 1) differential-thermal analysis; 2) thermogravimetric analysis.

Direct elimination of an ammonia molecule from compounds Ia, b, ethanol from Ic, d, and hydrogen sulfide from Ie, f takes place in the first fragmentation stage or step, as evidenced by their metastable ion spectra (using the DADI method) and their high resolution mass spectra (HRMS, Table 1). The observed decay process is accompanied by intramolecular condensation of compounds Ia-f and the formation of a tricyclic triazolo[1,5-*a*]pyrido[2,3-d]pyrimidine type heterosystem IIa-d.*



II a R=H, Z=O; b R=CH_3, Z=O; c R=H, Z=NH; d R=CH_3, Z=NH

We propose, therefore, that the EI-MS of compounds Ia-f represent in principle the spectra of mixtures of two substances: the original 2-triazolylaminopyridines and their intramolecular condensation products (compounds IIa-d), the latter forming during mass spectral acquisition.

In order to study the thermal behavior of compounds Ia-f derivatives Ib, c, e were subjected to thermogravimetric analysis (Fig. 1).

It is clear from the nature of their differential thermal analysis (DTA) curves that in the temperature range 250-290°C an endothermic maximum is observed, which is accompanied by a mass loss or reduction of 5.4 mg in the sample; this mass represents 6% of the sample weight and corresponds, therefore, to elimination of one molecule of ammonia from compound Ib. Elimination of an ethanol molecule and subsequent intramolecular condensation of compound Ic occurs in the temperature range 120-130°C. The analogous process for elimination of a hydrogen sulfide molecule from Ie proceeds at 225°C. Loss of hydrogen sulfide further implies that the thioamide substituent is present in the thiol form.

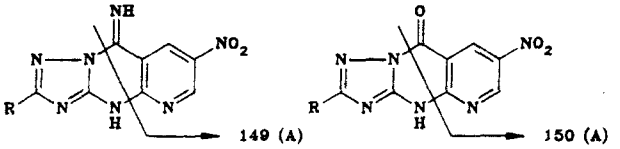
The feasibility of the thermal occurrence of this type of intramolecular condensation process for compounds Ia-f (EI-MS and thermogravimetry) was further verified by the experimental synthesis of the corresponding compounds IIa-d. Prolonged reflux of compounds Ia-f in DMF resulted in the practically quantitative recovery of their intramolecular condensation products, type-II tricyclic compounds. Thermolysis of the 1-azolylaminopyridines resulted in the formation of triazolo[1,5-*a*]pyrido[2,3-d]pyrimidines IIa, b (Z = O). After elimination of H_2S from compounds Ie, f amino derivatives of the same heterocyclic system are formed, namely IIc, d (Z = NH). The PMR and ^{13}C-NMR spectra of compounds IIa-c are superimposable with the corresponding spectra of triazolo[1-5*a*]pyrido[2,3-d]pyrimidines prepared via intramolecular condensation of compounds Ia-f upon treatment with bases [12].

The EI-MS of compounds IIa-d (Table 2) contain M^+ peaks, at maximum intensity, as well as discharged ion peaks M^{2+}, which is an accepted mass spectral index or characteristic of condensed heterosystems. The molecular or empirical composition of their M^+ ions was confirmed by HRMS measurements. The primary fragmentation step (according to the DADI procedure) appears to be fragmentation of compounds IIa, b and IIc, d via pathway A, resulting in the formation of ions with m/e 149 and 150, respectively; the empirical composition of these ions was also confirmed by HRMS (for IIa, b found 149.0229; calculated for $C_6H_3N_3O_2$ 149.0225; for IIc, d, found 150.0061; calculated for the empirical composition $C_6H_2N_2O_3$ 150.0065). The presence of these ions substantiates that compounds IIa-d exist predominantly in their oxo- and imino-forms; this is also supported by the observed loss of CO (from compounds IIa, b) and HCN from the $[M-NO_2]^+$ ion (for compounds IIc, d) (see scheme on following page).

*Compounds Ia, c and Ib, d give identical products, IIa and IIb, respectively.

TABLE 2. Mass Spectra of Compounds IIa-d

Compound	m/e (I, %)					
	$[M-NO]^+$	$[M-NO_2]^+$ Φ_1	$[\Phi_1-CZ]^+$	$[\Phi_1-RCN]^+$	Φ_A	rest of the spectrum
IIa	202 (3,1)	186 (17,6)	158 (7,4)	159 (8,3)	150 (8,3)	149 (13), 104 (10), 77 (14), 76 (24), 75 (12), 71 (18)
IIb	216 (2,6)	200 (41,1)	172 (12,3)	159 (4,4)	150 (15,0)	149 (41), 118 (10), 104 (19), 103 (22), 83 (18), 77 (21), 76 (54), 75 (25)
IIc	201 (10,3)	185 (45,4)	158 (22,6)	158 (22,6)	149 (22,3)	144 (10), 131 (13), 103 (33), 102 (17), 76 (40)
IId	215 (24,8)	199 (38,3)	172 (7,5)	158 (1,7)	149 (33,5)	103 (22), 102 (11), 85 (12), 82 (15), 76 (25), 71 (24)



The presence of $[M-NO]^+$ and $[M-NO_2]^+$ ion peaks in these spectra is characteristic of the presence of a nitro group in compounds IIa-d. The combination of mass spectrometric data examined herein is sufficient to verify the structure of compound II. However, we cannot exclude the possibility that compounds II actually exist in the form of other prototropic forms. The solution to this question will be the subject of a separate communication.

In conclusion, the results of our mass spectrometric study have enabled us to predict and verify experimentally a novel thermal intramolecular condensation pathway, leading to derivatives of the triazolo[1,5-*a*]pyridino[2,3-d]pyrimidine heterocyclic system.

EXPERIMENTAL

Mass spectra were measured on a Varian MAT-311 A spectrometer. The accelerating voltage was 3 kV, the cathode emission current 1 mA, the ionizing electron energy 70 eV. Samples were introduced to the ion source causing a direct injection procedure.

Thermal derivatograms were recorded on a Paulik–Paulik–Erdey thermal analyzer, using the following sample weights: 90 mg of Ib, 113 mg of Ic, and 80 mg of Ie. The time for one revolution of the cylinder was 50 min, the DTA sensitivity 1/5, the rate of heating 10°C/min, the standard Al_2O_3.

7-Nitro-9-oxo-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrido[2,3-d]pyrimidines (IIa, b). A solution of 0.01 moles 2-triazolylamino-3-carbamino-5-nitropyridine Ia, b or 2-triazolylamino-3-carboethoxy-5-nitropyridine Ic, d in 20 ml DMF was refluxed for 3 h, cooled, diluted with 80 ml water, and the resulting precipitate was removed by filtration. Yield of IIa, 96%; IIb, 94%.

7-Nitro-9-imino-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrido[2,3-d]pyrimidines (IIc, d). Prepared in an analogous manner by refluxing in DMF. Yield of compound IIc, 97%; IId, 93%.

The properties of compounds IIa-d were identical to the characteristics obtained for 1,2,4-triazolo[1,5-*a*]pyrido[2,3-d]pyrimidines prepared according to [12].

LITERATURE CITED

1. O. N. Chupakhin, V. G. Baklykov, N. A. Klyuev, and A. I. Matern, *Khim. Geterotsikl. Soedin.*, No. 8, 1083 (1989).
2. H. Schwarz, *Top. Curr. Chem.*, 73, 231 (1978).
3. Yu. V. Shurukhin, N. A. Klyuev, and I. I. Grandberg, *Khim. Geterotsikl. Soedin.*, No. 6, 723 (1985).
4. Yu. V. Shurukhin, N. A. Klyuev, and I. I. Grandberg, *Zh. Org. Khim.*, 21, 2057 (1985).
5. Yu. V. Shurukhin, N. A. Klyuev, and I. I. Grandberg, *Khim. Geterotsikl. Soedin.*, No. 7, 908 (1986).

6. Yu. V. Shurukhin, N. A. Klyuev, and I. I. Grandberg, *Zh. Org. Khim.*, **23**, 1063 (1986).
7. N. A. Klyuev, V. G. Baklykov, V. N. Charushin, and O. N. Chupakhin, *Khim. Geterotsikl. Soedin.*, No. 4, 532 (1989).
8. K. Tetsuji, *J. Pharm. Soc. Jpn.*, **101**, 1 (1981).
9. S. Meyerson, *Chem. Technol.*, **9**, 560 (1979).
10. V. L. Rusinov, T. L. Pilicheva, A. A. Tumashov, and O. N. Chupakhin, *Khim. Geterotsikl. Soedin.*, No. 6, 857 (1987).
11. V. L. Rusinov, T. L. Pilicheva, A. A. Tumashov, G. G. Aleksandrov, E. O. Sidorov, and I. V. Karpin, *Khim. Geterotsikl. Soedin.*, No. 12, 1632 (1990).
12. O. N. Chupakhin, V. L. Rusinov, A. A. Tumashov, T. L. Pilicheva, E. O. Sidorov, and I. V. Karpin, *Khim. Geterotsikl. Soedin.*, No. 2 (1991) (in press).
13. Yu. P. Chikishev, N. A. Klyuev, V. G. Zhil'nikov, and É. N. Istratov, Kauchuk Rezina, No. 4, 51 (1976).
14. N. A. Klyuev, Yu. V. Shurukhin, V. A. Konchits, I. I. Grandberg, V. L. Rusinov, V. A. Zyryanov, and I. Ya. Postovskii, *Khim. Geterotsikl. Soedin.*, No. 2, 265 (1980).

CARBOCYCLE ANNELATED 1,2,4-TRIAZOLO[1,5-*a*]PYRIMIDINES

S. M. Desenko, Kh. Éstrada, V. D. Orlov, and O. A. Ponomarev

UDC 547.859.1'792.3'514.472'592: 543.422'426

Reaction of 3-amino-1,2,4-triazole with mono- and dibenzalcycloalkanones gives 4,7-dihydro-1,2,4-triazolo[1,5-a]pyrimidines annelated by five-, six-, or seven-membered carbocycles. They can be dehydrogenated to the corresponding heteraromatics. The spectro-luminescent properties of the compounds obtained are discussed.

We have previously reported [1] a method for synthesis of 4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines based on the condensation of 3-amino-1,2,4-triazole with α,β-unsaturated ketones. However, as is known [2, 3], cyclic unsaturated cyclic ketones which have a rigid s-cis structure are characterized by a sharply lowered reactivity toward many binucleophiles (hydrazine, aromatic and heteroaromatic o-diamines). Thus, the use of these ketones in the synthesis of heterocyclic systems is limited. The aim of this work was to investigate the cyclocondensation of 3-amino-1,2,4-triazole (I) with the mono- and dibenzalcycloalkanones II-IV.

Refluxing solutions of amine I and ketones II-IV for 0.5-2 h in DMF gives the annelated carbocycles of the dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines V-VII. Comparison of the target compound yields and the reaction times (Table 1) as determined by us with those given in [1] points to the absence of a significant lowering of the reactivity of ketones II-IV when compared with their acyclic analogs. Thus, the condensation of 3-amino-1,2,4-triazole with α,β-unsaturated ketones is less sensitive to the geometry of the enone fragment than analogous reactions based on 1,2- and 1,4-binucleophiles [2, 3] (see scheme below).

It should be mentioned that the highest reactivity among the ketones IVa-c is observed for 2-benzal-1-indanone (IVa) which requires only a 0.5-h reaction time with amine I (instead of the 1.5 h needed for ketones IVb, c). Lowering of the reac-

A. M. Gorki State University, Kharkov 310077. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 105-108, January, 1991. Original article submitted June 1, 1989.

 0009-3122/91/2701-0088$12.50