NITROAZINES.

19*. PROTOTROPIC TAUTOMERISM IN 6—NITRO—7—OXO—4,7—DIHYDRO—1,2,4—TRIAZOLO[5,1—*c*][1,2,4]TRIAZINES

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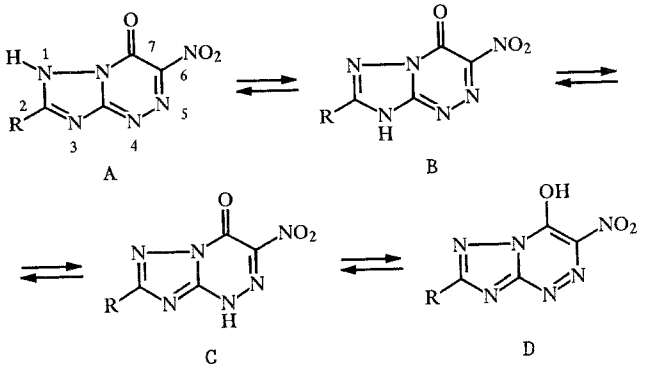
Prototropic reactions of 6—nitro—7—oxo—4,7—dihydro—1,2,4—triazolo[5,1—c][1,2,4]triazines is tautomeric as established from photoionization results. The ratios of the tautomers in the gas phase and in solution have been determined by mass and ^{13}C NMR spectroscopy.

Methylation of 6—nitro—7—oxo—4,7—dihydro—1,2,4—triazolo[5,1—*c*][1,2,4]triazines (I) gave 1—, 3—, and 4—methyl derivatives in the ratios 70—90 : 10—30 : 1—5 %. 3—Methyl— and 4—methyl—6—nitro—7—oxo—4,7—di-hydro—1,2,4—triazolo[5,1—*c*][1,2,4]triazines were isolated preparatively and characterized, but the O—methyl derivative was not observed [2]. The mixture of isomers formed indicates the presence of at least three (A—C) of the possible tautomers (isomers) in solution. As with the 2—hydroxypyridines and quinolines [3,4], the appearance of form D in the gas phase is not excluded.



Results of a study of the protropic rearrangements of compounds Ia—c and IIa and b in solution and in the gas phase are presented in this paper.

Model compounds III—VI, corresponding to the captured tautomeric forms, were made by methylation of the sodium salts of the nitrotriazines I and II by a published method [2].

Mass spectroscopy was used to determine the prototropic forms in the gas phase.

In the first stage of investigating the tautomerism of compounds I and II it was necessary to estimate the height of the activation barrier ($\Delta G^{=}$) to transition from one form to another to decide whether tautomerism or isomerism and to determine the characteristic criteria which permit the identification of one form or another.

Photoionisation results were used to measure the energy parameters associated with the transition from one form to another. The difference in ionization energies (IE) between the fixed (captured) forms in compounds IIIb and Vb is 0.31 ± 0.03 eV (29.91 kJ/mol) (Table 1) which shows that the rearrangement is tautomeric ($\Delta G^{=}$ 80—100 kJ/mol [3] for isomers).

*For Communication 18 see [1].

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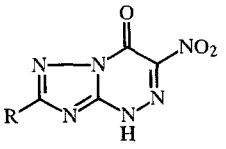
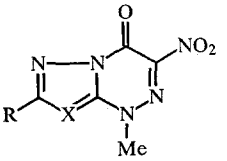
TABLE 1

Compound	Ionization energy, eV.	Compound	Ionization energy, eV
Ia	9,20 ± 0,03	IIIb	9,12 ± 0,03
Ib	9,45 ± 0,03	IIIc	8,72 ± 0,03
Ic	8,80 ± 0,02	Vb	8,81 ± 0,03

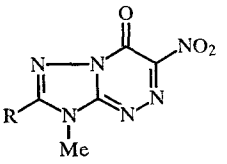
The introduction of a methyl group into an aryl or heteroaryl ring is known to decrease the IE by 0.2—0.5 eV. Bearing this in mind, the IE values observed for compounds Ib and Ic are close to that for form C which allows the assumption that this form is dominant in the gas phase.



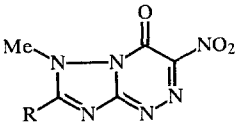
Ia-c, IIa, b



IIIa-c, IVa, b



Va, b



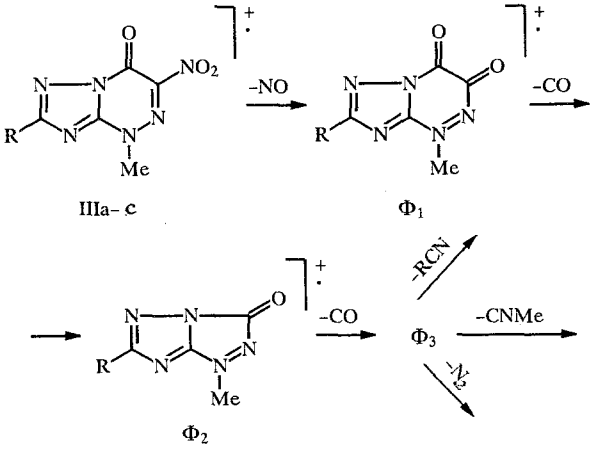
VIa, b

I, III X = N; II, IV X = CH a R = H; b R = CH_3; c R = SCH_3

The basic fragmentation pathway in the model 4—methyl—6—nitro—7—oxo—4,7—dihydroazolo[5,1—c][1,2,4]triazines IIIa—c, IVa and IVb is connected with elimination of NO and two CO units from the molecular ion to give fragments Φ_1 to Φ_3. Further decomposition of ion Φ_3 occurs with ejection of a further CO (with subsequent elimination of RCH, CNMe, and N_2)* (scheme 1, Table 2).

3—Methyl derivatives (captured form C) behave quite differently under electron impact. The first step in the fragmentation of 3—methyl—6—nitro—7—oxo—1,2,4—triazolo[5,1—*c*][1,2,4]triazines Va and Vb is elimination of a nitro group from the molecular ion to give ion Φ_4 (scheme 2, Table 2) which is the maximal ion in the spectra. Further decomposition involves loss of CO to give ion Φ_5 which apparently rearranges (possibly to an eight membered ring) and this facilitates direct loss of the fragments N_2C_2H, $N_3C_2H_2$, and N_3CR. The fragmentation pathway associated with loss of NO is completely absent. [M−NO] fragments are not observed. Mass spectra of mixtures of the 1— and 3—isomers (Va,b + VIa,b) shows that fragmentation pathways of the 1— and 3—H tautomers are the same after formation of the rearranged ion.

Scheme 1



* The nature of the decomposition was confirmed by metastable ion spectra (DADI).

TABLE 2. Mass Spectra of Compounds I—V

Compound	m/z (I_{rel}, %)						
	$[M+1]^+$	M^+	$[M-NO]^+$	$[M-NO_2]^+$	$[\Phi_1-CO]^+$	$[\Phi_4-CO]^+$	$[\Phi_2-CO]^+$
Ia	183(8)	182(100)	152(2)	136(4)	124(4)	109(5)	96(7)
Ib	197(8)	196(100)	166(4)	—	—	—	110(8)
Ic	229(6)	228(47)	198(5)	182(9)	170(3)	154(7)	—
IIa	182(8)	181(100)	151(7)	—	123(15)	—	—
IIb	196(8)	195(100	165(4)	—	137(4)	—	—
IIIa	197(8)	196(100)	166(6)	—	138(12)	—	110(23)
IIIb	211(9)	210(100)	180(5)	—	152(11)	—	124(20)
IIIc	243(12)	242(53)	212(4)	—	184(10)	—	156(16)
IVa	196(7)	195(83)	165(4)	—	137(15)	—	—
IVb	210(9)	209(100)	179(3)	—	151(14)	—	—
Va	197(7)	196(96)	—	150(100)	—	122(13)	—
Vb	211(7)	210(74)	—	164(100)	—	136(24)	—

TABLE 3. ^{13}C NMR Spectra of Compounds Ia,b — VIa,b

Compound	Chemical shift, δ, ppm, $^{13}C-^{1}H$ splitting pattern (J, Hz)						
	$C_{(2)}$	$C_{(3)}$	$C_{(CH3)}$	$C_{(3a)}$	$C_{(NCH3)}$	$C_{(6)}$	$C_{(7)}$
Ia	154,60 d (^1J=213)			154,26 d (^3J=9)		144,14	144,56
IIa	146,12 d.d (^1J=190, ^2J=5)	92,56 d.d (^1J=185, ^2J=11)		143,91 d.d (^2J=11, ^3J=7)		139,70	143,91
IIIa	155,33 d (^1J=214)			152,97 dq (^2J=9, ^3J=2)	43,58 d (^1J=145)	141,62	144,24
IVa*	146,04 d.d (^1J=191, ^2J=5)	93,67 d.d (^1J=185, ^2J=11)		144,07 dq	44,80 q (^1J=144)	138,05	143,23
Va	147,38 dq (^1J=224, ^3J=3)			151,28 dq (^3J=6, ^3J=3)	32,32 q (^1J=145)	150,20	142,90
VIa	155,37 dq (^1J=213, ^3J=3)				53,91 q (^1J=144)		
Ib	163,18 q (^2J=7)		14,72 q (^1J=130)	153,89		144,82	143,83
IIIb	165,22 q (^3J=7)		15,26 (^1J=129)	153,04 q (^3J=2)	43,50 q (^1J=145)	141,66	143,75
Vb	156,23 q		11,24	152,12	30,84	150,37	142,37
VIb**			15,23		49,48		

* A spectrum of a mixture with isomer Va was recorded. Signals of the quaternary carbon atoms were not observed because of the low concentration.

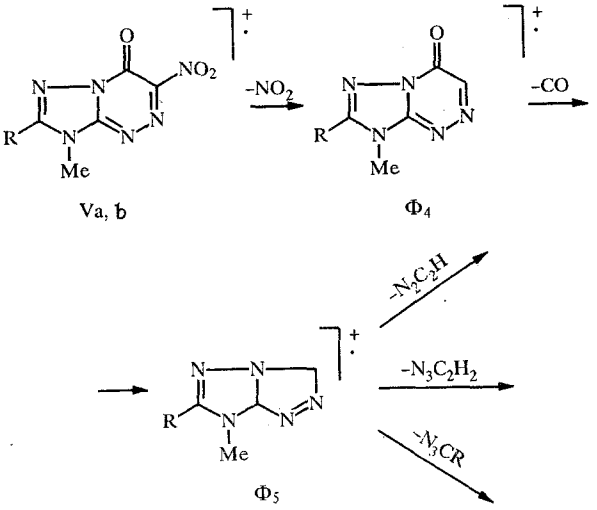
** A spectrum of a mixture with isomer Vb was recorded. Signals of the quaternary carbon atoms were not observed because of the low concentration.

The observed differences in fragmentation of the model compounds III—V even at the stage of formation of the first fragment ions permitted the identification and quantitative estimation of the tautomeric forms in the experimental compounds by mass spectroscopy.

It should be noted that fragmentation processes characteristic of form D, i.e. loss of an H atom (α—scission relative to the heteroaryl nucleus) and COH and NO_2H fragments (an *ortho*—effect) from M^+ were not observed during analysis of the mass spectra of compounds Ia—c, IIa and IIb (Table 2) so that this form does not exist in the gas phase.

Electron impact induced fragmentation of compounds Ib, IIa, and IIb coincide completely with the fragmentation of the 4—methyl derivatives IIIb, IVa, and IVb. No $[M-NO_2]^+$ peaks, characteristic of the 3—methyl derivatives, occur in their spectra. Hence these compounds exist in the gas phase predominantly in the C form which is confirmed by the photoionization results. The mass spectra of the triazolotriazines Ia and Ic contain ions corresponding to both form B ($[M-NO_2]^+$, $[M-NO_2-CO]^+$) and form C (Φ_1, Φ_2, Φ_3) (schemes 1 and 2, Table 2).

Analysis of prototropic forms in solution was carried out by ^{13}C and ^{1}H NMR spectroscopy.



In the ^{13}C NMR spectra of the model 1—, 3—, and 4—methyl derivatives IIIa—c, IVa, Va, Vb, VIa and VIb the position of the methyl group affects the chemical shifts of the carbon atoms of the skeleton, the most affected being atoms $C_{(2)}$ and $C_{(3a)}$ (Table 3). Comparison of the carbon spectra of these model compounds with those of Ia—c and IIa showed that the chemical shifts of skeletal C atoms in the N—H forms of I and II were close in value to the corresponding chemical shifts of the N_4—methyl derivatives III. The chemical shifts of the N_1 isomers VI are also close but, considering their negligible yield [2], it may be concluded that azolo—1,2,4—triazines I and II exist in DMSO solution, as in the gas phase, predominantly in the 6—nitro—7—oxo—4,7—dihydroazolo[5,1—*c*][1,2,4]triazine structure (form C). This confirms calculations of the mole fraction of tautomeric form C (N_C) based on a known expression [5] for rapid exchange between two particles:

$$N_C = \frac{\delta_{i(I)} - \delta_{i(IV)}}{\delta_{i(III)} - \delta_{i(IV)}},$$

where $\delta_{i(I)}$, $\delta_{i(III)}$, and $\delta_{i(IV)}$ are the chemical shifts for carbon atoms (C_2 or C_5) for compounds I, II, and III respectively.

Calculation based on the chemical shifts of C_2 gave values of $N_C = 0.91$ for Ia and $N_C = 0.77$ for Ib.

EXPERIMENTAL

EI Mass spectra were recorded with a Varian MAT—311A machine with indirect insertion of the sample into the ion source with an ionization energy of 70 eV. Photoionization was carried out in an MS—1302 mass spectrometer with a hydrogen lamp as source of the ionizing photons. Ionization curves were recorded simultaneously with the optical spectrum of the hydrogen lamp in the energy range 6—13 eV. Ionization energies were determined as the value of the photoion energy of the crest of the photoionization effectiveness curve with a precision of ± 0.02.

NMR spectra were recorded on a Bruker WH—90 spectrometer (22.62 MHz) in DMSO—D_6 with dioxane as internal standard.

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