EXPERIMENTAL

The mass spectra of the investigated compounds were obtained with an MKh-1303 spectrometer with a system for direct introduction of the samples at an ionizing energy of 50 V and an emission current of 1.5 μA at temperatures 20-40° below the melting points of the substances. The high-resolution mass spectrum of I was obtained with a JEOL JMS-01-SG-2 mass spectrometer. The IR spectra of the compounds were recorded with an IKS-22 spectrometer. The UV spectra were recorded with the Specord UV-vis spectrophotometer. Polarographic reduction was carried out under the conditions described in [4].

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CYCLIZATION OF N^1-ARYL-N^3-ACETYL-p-NITROBENZAMIDRAZONES TO SUBSTITUTED 1,2,4-TRIAZOLES

M. O. Lozinskii, T. N. Kudrya,
S. V. Bonadyk, and P. S. Pel'kis

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The reaction of α-acetamido-p-nitroacetophenone with benzenediazonium salts gave N^1-aryl-N^3-acetyl-p-nitrobenzamidrazones, which are cyclized to 5-methyl-1-aryl-3-(p-nitrobenzoyl)-1,2,4-triazoles. The latter are quaternized at the nitrogen atom in the 4 position.

α-Acetamido-p-nitroacetophenone (I) is used as an intermediate in the synthesis of levomycetin [1]. Little study has been devoted to its chemical properties; in particular, its reactions at the active methylene group have not been investigated.

In the present research we studied the reaction of I with arenediazonium salts and showed that the products are N^1-aryl-N^3-acetyl-p-benzamidrazones (II). In the case of electron-donor substituents in the benzenediazonium salts the yields of II are close to quantitative, whereas in the case of electron-acceptor substituents (chloro and nitro groups) one observes the formation of a complex mixture of products, from which we were able to isolate, in addition to the amidrazone, a side product – 1,5-bis(p-chlorophenyl)-3-acetamidoformazan (VIII) – in the case of p-chlorobenzenediazonium chloride.

Compound II (Table 1) has the properties of polymorphism and phototropy. The UV spectra of IIa-h contain absorption maxima at 230-270 and 380-400 nm. Characteristic bands at 1580-1620 (C = N), 1670 and 1630 (C = O), and 3280-3340 cm^{-1} (NH) are observed in the IR spectra, and this confirms their hydrazone structure [2].

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TABLE 1. N^1-Aryl-N^3-acetyl-p-nitrobenzamidrazones II

Compound	mp, °C	N found, %	Empirical formula	N calc., %	Yield, %
IIa	159	17,2	$C_{16}H_{14}N_4O_4$	17,1	84
IIb	168—170	16,4	$C_{17}H_{16}N_4O_4$	16,4	82
IIc	165—166	16,4	$C_{17}H_{16}N_4O_4$	16,4	100
IId	163—164	16,4	$C_{17}H_{16}N_4O_4$	16,4	71
IIe	165—166	15,7	$C_{17}H_{16}N_4O_5$	15,7	80
IIf	166—168	15,4	$C_{16}H_{13}ClN_4O_4$*	15,5	58
IIg	240—242	18,8	$C_{16}H_{13}N_5O_6$	18,9	60
IIh	166—167	15,9	$C_{18}H_{18}N_4O_4$	15,8	100

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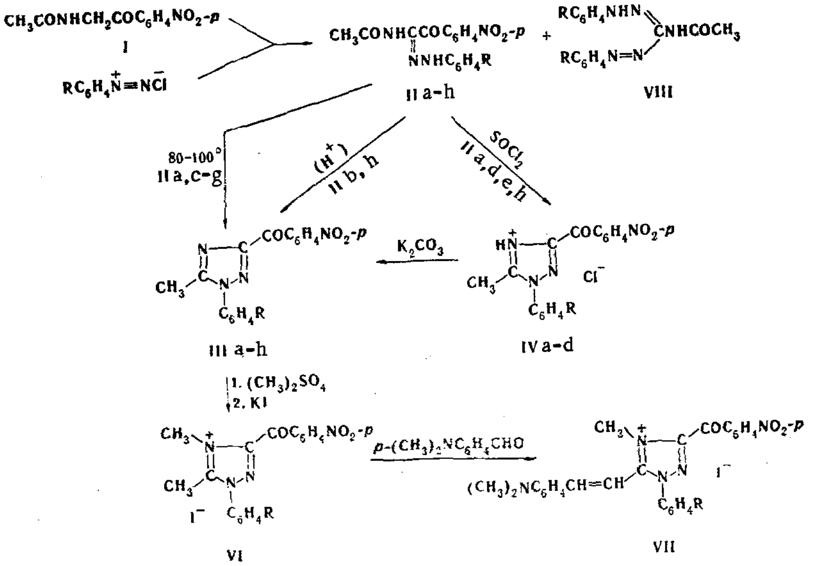
* Found: C 53.4; H 3.7; Cl 9.3%. Calculated: C 53.2; H 3.6; Cl 9.7%.

TABLE 2. 5-Methyl-1-aryl-3-(p-nitrobenzoyl)-1,2,4-triazoles III

Compound	mp, °C	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
IIIa	172	62,3	3,6	18,2	$C_{16}H_{12}N_4O_3$	62,4	3,9	18,2	100
IIIb	133—134	63,5	4,3	17,1	$C_{17}H_{14}N_4O_3$	63,4	4,3	17,4	99
IIIc	115	63,5	4,2	17,5	$C_{17}H_{14}N_4O_3$	63,4	4,3	17,4	98
IIId	142—143	63,3	4,3	17,2	$C_{17}H_{14}N_4O_3$	63,4	4,3	17,4	100
IIIe	127	60,0	4,0	16,6	$C_{17}H_{14}N_4O_4$	60,3	4,1	16,6	98
IIIf	151	53,4	3,7	15,4	$C_{16}H_{11}ClN_4O_3$	53,2	3,6	15,5	60
IIIg	134—135	—	—	19,9	$C_{16}H_{11}N_5O_5$	—	—	19,8	98
IIIh	180—181	—	—	16,5	$C_{18}H_{16}N_4O_3$	—	—	16,5	99

TABLE 3. 5-Methyl-1-aryl-3-(p-nitrobenzoyl)-1,2,4-triazolium Hydrochlorides

Compound	mp, °C	Cl found, %	Empirical formula	Cl calc., %	Yield, %
IVa	156—157	10,1	$C_{16}H_{13}ClN_4O_3$	10,3	73
IVb	179—180	9,8	$C_{17}H_{15}ClN_4O_3$	9,9	84
IVc	167—169	9,3	$C_{17}H_{15}ClN_4O_4$	9,5	100
IVd	151—152	10,8	$C_{18}H_{17}ClN_4O_3$	10.9	48



II, III a R=H; b R=*o*-CH₃; c R=*m*-CH₃; d R=*p*-CH₃; e R=*p*-CH₃O; f R=*p*-Cl; g R=*p*-NO₂; h R=2,4(CH₃)₂; IV a R=H; b R=*p*-CH₃; c R=*p*-CH₃O; d R=2,4(CH₃)₂; VIII R=*p*-Cl

When IIa,c-g are heated in alcohol or dioxane they split out a molecule of water and are readily converted to the previously undescribed 5-methyl-1-aryl-3-(p-nitrobenzoyl)-1,2,4-triazoles (Table 2): However, IIb,h undergo cyclization only in the presence of alkalines or acids; this is due to the steric hindrance created by the substituents in the ortho position of the corresponding amidrazone molecule, as seen from Stuart-Briegleb models. Treatment of IIa,d,e,h with thionyl chloride in benzene gave, instead of the expected imidoyl chlorides, 5-methyl-1-aryl-3-(p-nitrobenzoyl)-1,2,4-triazolium hydrochlorides (Table 3), which were converted to bases IVa-d.

The UV spectra of IIIa-h contain one absorption maximum at 270-275 nm (log ε 4.05-4.29); this is characteristic for triazole derivatives [3]. The IR spectra of the triazoles do not contain bands of the stretching vibrations of an NH bond at 3280-3240 cm^{-1}, and there is only one band at 1670 cm^{-1} in the region of carbonyl group absorption. Bands at 1400-1450 and 1100-1150 cm^{-1} are characteristic for the vibrations of the triazole ring [4].

It is well known that 1,3,5-trimethyl-substituted triazoles are methylated in the 4 position by methyl iodide [5]. We have established that methylation of 5-methyl-1-phenyl-3-(p-nitrobenzoyl)-1,2,4-triazole with dimethyl sulfate yields V, which forms the corresponding iodide VI when it is treated with potassium iodide. Proof for the formation of this product is provided by the introduction of a methyl group in the 5 position on condensation with p-dimethylaminobenzaldehyde to give VII.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The UV spectra of $3.6 \cdot 10^{-5}$ M alcohol solutions of the compounds were measured with an SF-4 spectrophotometer.

N^1-(p-Chlorophenyl)-N^3-acetyl-p-nitrobenzamidrazone (IIf). An equivalent amount of p-chlorobenzenediazonium chloride, obtained by the usual method, was added slowly at 0° to a solution of 0.03 mole of p-acetamido-p-nitroacetophenone and 25 g of sodium acetate in 75 ml of a mixture of pyridine and water (1:2), and the mixture was stirred for 2 h. The precipitate was removed by filtration, washed with water, dilute HCl, and water, and dried. Recrystallization from chloroform gave bright-orange crystals with a metallic luster. Compounds IIa-e,g,h were obtained by a similar method.

1,5-Bis(p-chlorophenyl)-3-acetamidoformazan (VIII). The chloroform mother liquor from the crystallization of IIf was chromatographed on Al_2O_3 [elution with chloroform–alcohol (50:1)], and the second zone was collected and worked up to give orange crystals with mp 195°. Found C 51.6; H 3.8; Cl 20.1; N 20.4%. $C_{15}H_{13}Cl_2N_5O$. Calculated: C 51.4; H 3.7; Cl 20.2; N 20.2%.

5-Methyl-1-phenyl-3-(p-nitrobenzoyl)-1,2,4-triazole (IIIa). A 0.01-mole sample of IIa was refluxed in 20 ml of dioxane for 30-45 min, and the resulting solution was cooled to give a precipitate of colorless crystals. The yield was quantitative. Compounds IIIc-g were obtained under similar conditions. The cyclization of IIb,h to IIIb,h was carried out for 1 h in the presence of a few drops of H_2SO_4.

5-Methyl-1-phenyl-3(p-nitrobenzoyl)-1,2,4-triazolium Hydrochloride(IVa). A 25-mmole sample of freshly distilled thionyl chloride was added to 5 mmole of IIa in 15 ml of benzene, and the mixture was refluxed for 35-40 min. The benzene was then removed by distillation, and the residue was crystallized from acetone to give IVa in 73% yield. Compounds IVb-d were similarly obtained. Treatment of IVa-d with aqueous $NaHCO_3$ solution gave the free bases, which did not depress the melting points of IIIa,d,e,h.

4,5-Dimethyl-1-phenyl-3-(p-nitrobenzoyl)-1,2,4-triazolium Metasulfate (V). A 1-g (3 mmole) sample of IIIa was mixed with 3.7 g (21 mmole) of dimethyl sulfate, during which the mixture heated up markedly, and an oily product formed. To complete the reaction, the mixture was heated on a water bath for 1 h. The oily product was triturated throughly with benzene, washed with absolute ether, and dried to give colorless crystals of V, with mp 65°, in 70% yield. Found: N 12.2; S 7.6%. $C_{18}H_{18}N_4O_7S$. Calculated: N 12.9; S 7.4%.

4,5-Dimethyl-1-phenyl-3-(p-nitrobenzoyl)-1,2,4-triazolium Iodide (VI). This compound was obtained by an exchange reaction of V with a saturated aqueous solution of potassium iodide. The yield was quantitative. The product had mp 170° (from water). Found: I 28.0; N 12.4%. $C_{17}H_{15}IN_4O_3$. Calculated: I 28.2; N 12.4%.

4-Methyl-1-phenyl-3-(p-nitrobenzoyl)-5-(p-dimethylaminostyryl)-1,2,4-triazolium Iodide (VII). A mixture of 5 mmole of VI, 5 mmole of p-dimethylaminobenzaldehyde, 5 mmole of dry triethylamine, and 5 ml of acetic anhydride was heated until the precipitated triazolium iodide vanished (3.5-4 h), and the oily product was separated and washed repeatedly with water until it was neutral. The product was triturated for a long time with water, as a result of which light-brown crystals with a metallic luster and mp 140-142° [from aqueous alcohol (1:10)] formed. Found: C 55.4; H 4.5%. $C_{26}H_{24}IN_5O_3$. Calculated: C 54.7; H 4.1%. UV spectrum, λ_{max}: 265 (340 nm).

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QUANTUM-CHEMICAL ANALYSIS OF THE TAUTOMERISIM OF 1,2,4-TRIAZOLE AND ITS AMINO AND DIAMINO DERIVATIVES

V. V. Makarskii, V. A. Zubkov,
V. A. Lopyrev, and M. G. Voronkov

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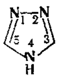
Calculation of the dipole moments and heats of formation for 1,2,4-triazole confirmed that it exists primarily in the unsymmetrical form, while similar calculations for 3-amino- and 3,5-diamino-1,2,4-triazoles showed that the amino tautomers with a hydrogen atom attached to the N–N bond are the preferred forms.

Despite the relatively large number of publications devoted to the tautomerism of 1,2,4-triazole (I), 3-amino-1,2,4-triazole (II), and 3,5-diamino-1,2,4-triazole (III), it is not completely clear which of the possible tautomeric forms of these compounds are actually realized. This is particularly true for the amino and diamino derivatives of 1,2,4-traiazole. This problem was studied in the present research by the methods of quantum chemistry.

X-ray diffraction analysis of 1,2,4-triazole (I) provides evidence [1,2] that in the crystalline phase, of the two possible tautomeric forms, planar unsymmetrical form IA is realized. Dipole moments ranging from 2.7 to 3.27 D have been obtained [3-5] for 1,2,4-triazole. The quantum-chemically calculated [5] dipole moment for IA is 3.07 D and is close to the experimental value. For solutions of 1,2,4-triazole in hexamethylphosphoric triamide, both the NMR data [6] and the method of fixed structures [7] provide evidence that form IA predominates.



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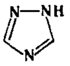

IA

The situation is less definite for amino derivatives II and III (there are five tautomeric forms with amino and imino structures; see below). The research involving the establishment of the structure of triazole II is of qualitative character and indicates the high probability of an amino structure (IIA-S) [8,9]. An amino–imino form (IIIC or IIID) has been proposed for guanazole III from the UV spectra [10]. It was later proposed that it has a diamino structure (IIIE) [11]. Infrared spectroscopy of guanazole before and after deuteration of the

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Leningrad Institute of the Textile and Light Industry, Leningrad 191065. Institute of High-Molecular-Weight Compounds, Academy of Sciences of the USSR, Leningrad 199004. Irkutsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Irkutsk 664033. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 540-545, April, 1977. Original article submitted May 23, 1976.