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3-Hydrazino-1,2,4-triazin-5(2*H*)-ones in Reactions with Compounds Containing Carbonyl and Active Methylene Groups

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Abstract—Boiling of ethyl cyanoacetate with 6-*tert*-butyl-3-hydrazino-1,2,4-triazin-5(2*H*)-one in alkaline medium yielded 6-*tert*-butyl-3-(5-hydroxy-3-oxo-2,3-dihydro-1*H*-pyrazol-1-yl)-1,2,4-triazin-5(2*H*)-one. Acylation of 6-*tert*-butyl-3-hydrazino-1,2,4-triazin-5(2*H*)-one with benzoyl chloride furnished 3-benzoylhydrazido-1,2,4-triazine that cyclized when treated with $POCl_3$ providing a derivative of [1,2,4]triazolo[4,3-*b*][1,2,4]triazine. Boiling of 6-*tert*-butyl-3-hydrazino-1,2,4-triazin-5(2*H*)-one in glacial acetic acid gave rise to diacetylated derivative whereas the boiling with acetic anhydride in an inert solvent afforded monoacetylated product.

Among derivatives of hydrazino-1,2,4-triazine compounds were those found possessing bactericidal and fungicidal activities [1]. We previously investigated reactions of carbonyl compounds, isocyanates, arenesulfonyl chlorides with substituted 5- and 6-hydrazino-1,2,4-triazines. It was established that under common reaction conditions a substitution took place at the hydrazino group resulting in the corresponding monohydrazino derivatives of 1,2,4-triazine. No heterocyclization at the triazine nitrogen atoms occurred due both to the reaction conditions and to the structure of the initial triazines. In extension of this study we investigated reactions of 3-hydrazino-1,2,4-triazine with carboxylic acids, acyl chlorides, acid anhydrides, and compounds with active methylene groups.

The initial 6-tert-butyl-3-hydrazino-1,2,4-triazin-5(2*H*)-one (**I**) was obtained by hydrazinolysis of 6-*tert*-butyl-3,4-dihydro-3-thioxo-1,2,4-triazin-5(2*H*)-one in alcohol along procedure [4].

After boiling ethyl cyanoacetate with compound **I** in alcoholic solution of potassium hydroxide was isolated 6-*tert*-butyl-3-(5-hydroxy-3-oxo-2,3-dihydro-1*H*-pyrazol-1-yl)-1,2,4-triazin-5(2*H*)-one (**II**). The ethyl cyanoacetate is known [5] to exist in the alkaline medium predominantly in an enol form. The attack of the nucleophilic site (amino group of the hydrazine substituent) occurred at the electrophilic site of the cyanoacetate enolate ion providing a tetrahedral intermediate that stabilized by eliminating ethanol. The cyanoacetic acid hydrazide cyclized at heating into the corresponding pyrazole derivative. Since in the reaction mixture was present water instead of the expected 3-(5-amino-3-oxo-2,3-dihydro-1*H*-pyrazol-1-yl)-6-*tert*-butyl-1,2,4-triazin-5(2*H*)-one compound **II** was isolated. It is also known [6] that the reaction of ethyl cyanoacetate with substituted hydrazines occurred with cyclization resulting in fused systems. Carrying out the reaction under the above described conditions (boiling in alcohol of a mixture of compound **I** and ethyl cyanoacetate) we did not succeed in isolating the expected triazolotriazine. In the mass spectrum of compound **II** the molecular ion peak was observed at *m/z* 251.

From the boiled solution of compound **I** and acetic anhydride in a nonpolar solvent a product of monoacetylation of triazolone **I**, *N*'-(6-*tert*-butyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)acetohydrazide (**IV**), was separated. whereas from the mixture of compound **I** and excess glacial acetic acid after boiling was isolated *N*'-acetyl-*N*-(6-*tert*-butyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)acetohydrazide (**III**) (see the scheme).

The heating at 80–85°C of compound **I** with excess freshly distilled benzoyl chloride gave rise to *N*'-(6-*tert*-butyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)-benzohydrazide (**V**). The reactions follow common mechanism of nucleophilic substitution, No acylation occurred at the nitrogen in the *2* position of the heterocycle as confirmed by the presence of proton singlets at 12.36, 12.35, and 12.16 in the ^{1}H NMR spectra of compounds **III**–**V** respectively.

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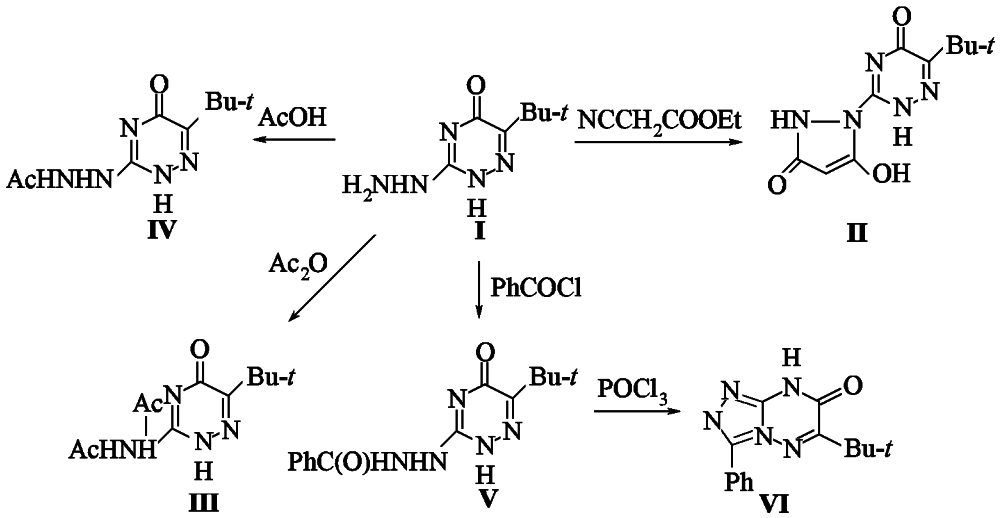
Scheme.



After boiling compound **V** with $POCl_3$ in an inert solvent was isolated 6-*tert*-butyl-3-phenyl[1,2,4]triazolo[4,3-b][1,2,4]triazin-7(1*H*)-one (**VI**) The bicyclic system originated from an intramolecular attack of a nucleophilic site (nitrogen atom in *2* position of the triazine ring) on the electrophilic site of the carbonyl group followed by water elimination from the tetrahedral intermediate. In the mass spectrum of this compound the molecular ion was observed at *m/z* 269. In its ^{1}H NMR spectrum the singlet of protons of the *tert*-butyl group appeared at 1.34 ppm, and the multiplet of phenyl protons at 7.33–7.77 ppm. In the IR spectrum of compound **VI** the stretching vibrations of the carbonyl group in the triazine ring give rise to the absorption band at 1714 cm^{-1} which is shifted to shortwave region compared to the spectrum of the initial compound **V**.

EXPERIMENTAL

IR spectra were registered on spectrophotometer UR-20 from KBr pellets. ^{1}H NMR spectra were measured on spectrometer Tesla BS-487B at operating frequency 80 MHZ, internal reference HMDS. Mass spectra were recorded on mass spectrometer MS-1302. The purity of reaction products was tested by TLC on Silufol UV-254 plates, eluent chloroform–acetone–benzene, 1 : 3 : 1.

Compound **I** was prepared by procedure [4], mp 270–271°C.

6-*tert*-Butyl-3-(5-hydroxy-3-oxo-2,3-dihydro-1*H*-pyrazol-1-yl)-1,2,4-triazin-5(2*H*)-one (II). To an alcohol solution of potassium hydroxide was added at stirring 1.83 g (0.01 mol) of compound **I**, 1.7 g (0.015 mol) of ethyl cyanoacetate, and the mixture was boiled for 5 h. The excess alcohol was distilled off on a water bath, the residue was cooled, several drops of glacial acetic acid were added thereto till pH 7, the precipitate was filtered off, dried in air, and recrystallized from 2-propanol to furnish 1.2 g (48%) of colorless crystalline substance, mp 201–202°C. Mass spectrum, *m/z*: 251 ($M^{+\cdot}$), 208, 153, 140, 125, 112, 99, 86, 68, 57, 42. Found, %: C 47.7; H 5.3; N 27.6. $C_{10}H_{13}N_5O_3$. Calculated, %: C 47.8; H 5.2; N 27.9.

***N*′-Acetyl-*N*-(6-*tert*-butyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)acetohydrazide (III).** In 10 ml of glacial acetic acid 1.83 g (0.01 mol) of compound **I** was boiled for 5 h. The reaction mixture was cooled, filtered, the filtrate was diluted with 20 ml of distilled water. The separated precipitate was filtered off, dried in air, and recrystallized from 2-propanol to furnish 2.4 g (84%) of colorless crystalline substance, mp 226–227°C. IR spectrum, ν, cm^{-1}: 1690, 1665 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.28 s (9H), 1.96 s (6H), 10.34 s (1H), 12.36 s (1H). Found, %: C 49.4; H 6.4; N 26.3. $C_{11}H_{17}N_5O_3$. Calculated, %: C 49.4; H 6.4; N 26.2.

***N*′-(6-*tert*-Butyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)acetohydrazide (IV).** A mixture of 1.83 g (0.01 mol) of compound **I**, 1.2 ml (0.01 mol) of acetic anhydride, and 20 ml of anhydrous benzene was boiled for 5 h. The hot mixture was filtered, excess benzene was removed in a vacuum. To the residue a mixture 2-propanol–water, 1 : 2, was added, the separated precipitate was filtered off, dried in air, and recrystallized from 2-propanol. We obtained 1.8 g (80%) of yellow crystalline substance, mp 221–

222°C. IR spectrum, ν, cm^{-1}: 1665, 1710 (C=O); 3210 (N–H). ^1H NMR spectrum, δ, ppm: 1.28 s (9H), 1.98 s (3H), 12.35 s (1H). Found, % : C 47.8; H 6.7; N 31.1. $C_9H_{15}N_5O_2$. Calculated, %: C 48.0; H 6.7; N 31.1.

***N'*-(6-*tert*-Butyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)benzohydrazide (V).** A mixture of 0.92 g (2 mmol) of compound **I** and 10 ml of benzoyl chloride was heated to boiling for 5 h. Then the reaction mixture was cooled, the precipitate was filtered off, dried in air, and recrystallized from a mixture 2-propanol–water, 1 : 2. We obtained 1.2 g (84%) of colorless crystalline compound, mp 223–224°C. IR spectrum, ν, cm^{-1}: 1665, 1725 (C=O). ^1H NMR spectrum, δ, ppm: 1.28 s (9H), 7.53–7.94 m (5H), 9.3 s (1H), 10.48 s (1H), 12.67 s (1H). Found,%: C 58.5; H 6.0; N 24.4. $C_{14}H_{17}N_5O_2$. Calculated,%: C 58.5; H 6.0; N 24.4.

6-***tert*-Butyl-3-phenyl[1,2,4]triazolo[4,3-b][1,2,4]triazin-7(1*H*)-one (VI).** A mixture of 0.57 g (2 mmol) of compound **V**, 2 ml of $POCl_3$, and 20 ml of anhydrous xylene was heated to boiling for 8 h. The excess solvent and $POCl_3$ was distilled off in a vacuum, and the residue was diluted with a mixture 2-propanol–water, 1 : 1., and left overnight. The precipitate was filtered off dried in air, and recrystallized from a mixture 2-propanol–water, 1 : 2. We obtained 0.36 g (67%) of colorless crystalline substance, mp 248–249°C. IR spectrum, ν, cm^{-1}: 1714 (C=O). ^1H NMR spectrum, δ, ppm: 1.34 s (9H), 7.33–7.77 m (5H), 9.8 s (1H). Mass spectrum, *m/z*: 269 ($M^{+\bullet}$), 254, 240, 226, 214, 199, 187, 173, 160, 146, 138, 129, 113, 104, 96, 77, 68, 57, 41. Found, %: C 62.5; H 5.6; N 26.3. C14H15N5O. Calculated, %: C 62.4; H 5.6; N 26.0.

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