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## ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

# Synthesis of 3-Pyridyl-substituted 5-Amino-1,2,4-triazoles from Aminoguanidine and Pyridinecarboxylic Acids

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**Abstract**—Effect of the molar ratio between reagents, temperature, and synthesis duration on the yield of 3-pyridyl-substituted 5-amino-1,2,4-triazoles in the reaction of aminoguanidine hydrochloride with pyridinecarboxylic acids under acid catalysis conditions was studied. A single-reactor method for synthesis of 3-pyridyl-substituted 5-amino-1,2,4-triazoles and their hydrochlorides was developed.

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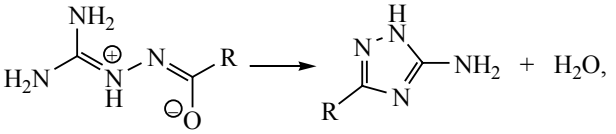
3-Pyridyl-substituted 5-amino-1,2,4-triazoles (**I**)–(**III**) and their derivatives are used as reagents for synthesis of various biologically active and medicinal substances [1–3] and coordination compounds [4–6]. Triazoles (**I**)–(**III**) are commonly produced by cyclization of 2-guanyl hydrazides (**IV**)–(**VI**) of the corresponding pyridinecarboxylic acids under their heating in the crystalline state [2, 7, 8], boiling in an aqueous solution [9], or under microwave heating [10]:



**IV**–**VI** **I**–**III**

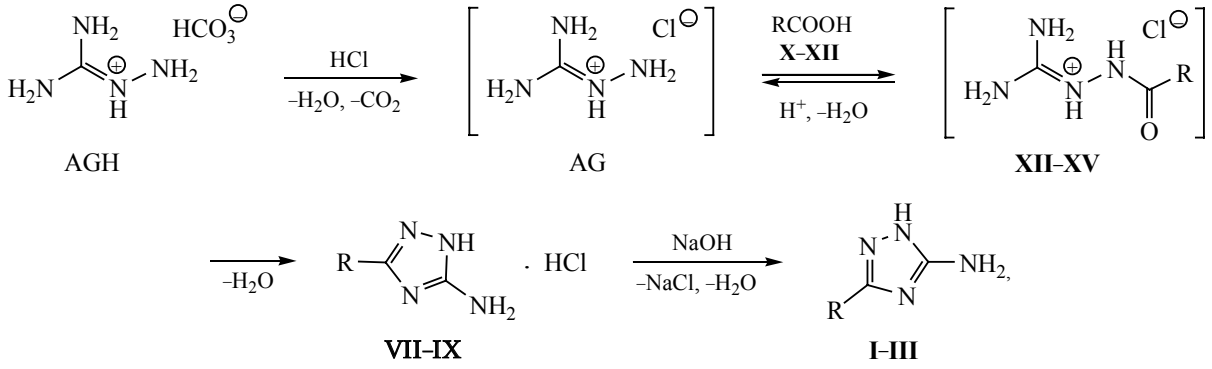
where R is 2-pyridyl (**I**), (**IV**); 3-pyridyl (**II**), (**V**); or 4-pyridyl (**III**), (**VI**).

The main disadvantage of this method is that the synthesis of the starting guanyl hydrazides (**IV**)–(**VI**) by the reaction of pyridinecarboxylic acid hydrazides with methylisothiourea sulfate is prolonged (3–4 days) and is accompanied by release of the toxic gaseous methyl mercaptan. An alternative way to synthesize guanyl hydrazides by fusion of pyridinecarboxylic acid chloroanhydrides with an excess amount of aminoguanidine hydrochloride [8] is also poorly efficient because of the high cost of the starting substances and loss of aminoguanidine in isolation of the product. Attempts have been made to synthesize compounds **I**–**III** in a single stage by reacting pyridinecarboxylic acids with aminoguanidine salts [2, 8, 11]. A rather high yield (90%) was observed in fusion of aminoguanidine sulfate (2 mol) with isonicotinic acid (1 mol) at 210°C [2]. Even though 1 mol of aminoguanidine is lost in isolation of the product, this example demonstrates that a single-stage synthesis of compounds **I**–**III** from aminoguanidine and pyridinecarboxylic acids can be developed.

In this communication, we describe a single-reactor method for synthesis of compounds **I**–**III** and their hydrochlorides **VII**–**IX** from aminoguanidine hydrocarbonate (AGH), hydrochloric acid, and pyridinecarboxylic acids **X**–**XII** by the scheme.

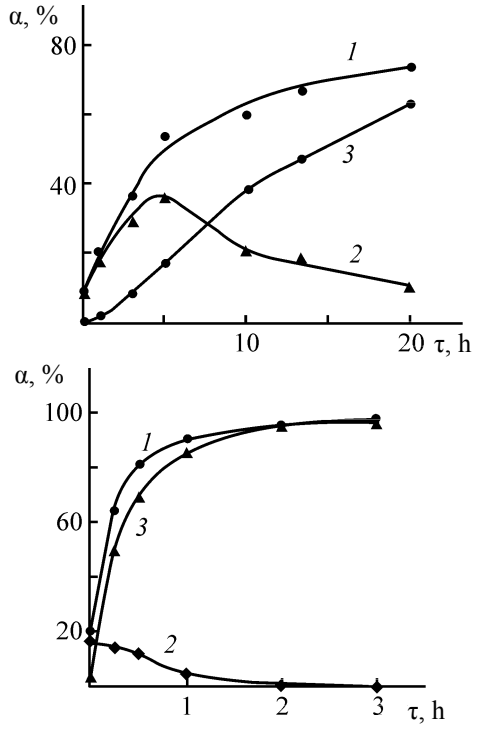
It has been shown previously [12–15] that the key stage in synthesis of 3-substituted 5-amino-1,2,4-triazoles from aminoguanidine and carboxylic acids is that in which guanyl hydrazides are formed. Because this reaction is acid-catalyzed, it is advisable to synthesize guanyl hydrazides at pH ≤ 1 and, for providing a high equilibrium conversion, to use concentrated solution with the minimum content of water, produced by mixing of AGH with a minor excess of $HCl_{conc}$ and carboxylic acid [13–15]. However, our attempt to synthesize guanyl hydrazides hydrochlorides **XIII**–**XV** under the conditions suggested in [13–15] failed.

**Scheme.**




where R is pyridin-2-yl (**I**), (**VII**), (**X**), (**XIII**); pyridin-3-yl (**II**), (**VIII**), (**XI**), (**XIV**); or pyridin-4-yl (**III**), (**IX**), (**XII**), (**XV**).

It was found that the effective rate constant $k'$ of the reaction of aminoguanidine with nicotinic acid at 80°C and pH 0.50 ± 0.01 is (2.1 ± 0.3) × $10^{-5}$ $M^{-1}$ $min^{-1}$, which is by three orders of magnitude lower than that for the reaction with acetic acid ($k'$ = 3.3 × $10^{-2}$ $M^{-1}$ $min^{-1}$, calculated from the data of [14]). Thus, because the reaction of aminoguanidine with pyridinecarboxylic acids is substantially slower than that with aliphatic carboxylic acids, the synthesis should be performed at a higher temperature.




Variation α of (*1*) AG conversion and yield of compounds (*2*) **XIV** and (*3*) **VII** with time τ at temperatures of (a) 135 and (b) 180°C.

As the reaction temperature is raised to 135–140°C (upon evaporation of water from the reaction mixture under atmospheric pressure), the reaction rate noticeably increases. However, compounds **XIII–XV** being formed are gradually cyclized at this temperature to aminotriazole hydrochlorides **VII–IX** (figure a). At temperatures of 180–200°C, the cyclization reaction is comparable in rate with the reaction in which guanyl hydrazides are formed (figure b; reactions with acids **X** and **XII** occur in a similar way). Consequently, it is advisable to obtain 3-pyridyl-substituted 5-amino-1,2,4-triazole hydrochlorides **VII–IX** from aminoguanidine and pyridinecarboxylic acids **X–XII** in a single preparative stage.

It can be seen in Table 1 that an excess of hydrochloric acid accelerates the reaction. Presumably, the excessive amount of HCl is bound with pyridinecarboxylic acid to give a salt playing the role of a catalyst. Use of a >30% excess of HCl changes the reaction rate only slightly and is inadvisable. The best yields of salts

**Table 1.** Effect of the initial AGH : HCl ratio on the conversion α of AG AGH : **XI** = 1 : 1 (mol : mol), 165°C

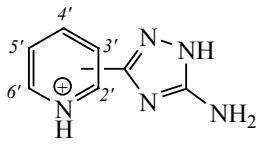
| AGH : HCl, mol : mol | α, %, at indicated synthesis duration, min | | | | |
|---|---|---|---|---|---|
| | 30 | 60 | 120 | 180 | 300 |
| 1 : 1.00 | 29 | 45 | 65 | 72 | 77 |
| 1 : 1.10 | 33 | 59 | 68 | 75 | 80 |
| 1 : 1.20 | 36 | 61 | 71 | 79 | 83 |
| 1 : 1.30 | 45 | 67 | 77 | 85 | 88 |
| 1 : 1.50 | 65 | 78 | 87 | 88 | 92 |
| 1 : 2.00 | 65 | 79 | 87 | 88 | 93 |

**VII–IX** were obtained at temperatures of 180–185°C in the course of 4–6 h. At lower temperatures, it was necessary to make the synthesis duration longer, and at higher temperatures, impurities contaminating the target product were formed.

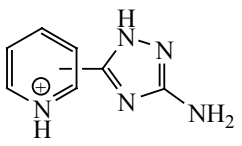
Thus, it can be recommended to perform the single-reactor synthesis of 3-pyridyl-substituted 5-amino-1,2,4-triazole hydrochlorides **VII–IX** under the following conditions: AGH : HCl : RCOOH molar ratio of 1 : 1.3 : 1, evaporation of water from the reaction mixture and heating at 180–185°C for 6 h. Upon crystallization from water, the yield of compounds **VII–IX** is 74–80%. When free triazoles **I–III** are synthesized, the heating duration can be diminished to 3 h, with the resulting fusion cake treated with aqueous alkalis for fast cyclization of guanyl hydrazides and formation of free aminotriazoles **I–III**. Upon neutralization and recrystallization from water, the yield of compounds **I–III** is 70–80%.

The structure of compounds **I–III** and **VII–IX** was confirmed by spectroscopic data and elemental analysis. $^1$H NMR spectra of compounds **I–III** are similar to those described in [10]. The spectrum of triazole **I** shows signals of two tautomers, **A** (5-amino-1*H*-1,2,4-triazole) and **B** (3-amino-1H-1,2,4-triazole) with close intensities and a tautomeric equilibrium constant $K_T$ = [**A**]/[**B**] = 1.7 (1.6 [10]). At the same time, only signals of tautomer **A** are detected in the spectra of compounds **II** and **III**.

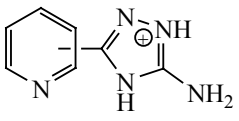
Of interest are structural features of salts **VII–IX**. In protonation of triazoles **I–III**, a proton can be added both to the nitrogen of the pyridine ring and to one of N atoms of the triazole ring. Taking into account the data on the tautomerism of C-amino-1,2,4-triazoles [10] and their salts with mineral acids, we can conclude that the tautomeric forms **A**, **B**, and **D** are the most probable for cations of salts **VII–IX**:




**A**




**B**




**D**

$^{13}$C NMR spectroscopy is an effective method for studying the tautomerism in C-amino-1,2,4-triazoles. The signal from nuclei of carbon atoms bonded to an amino group is characteristic and only slightly dependent on the substituent at another carbon atom of the triazole ring [10, 15–18]. The protonation of the pyridine moiety can be judged from the intensity of signals from C-2' and C-6', which are shifted upfield, compared with similar compounds containing an unprotonated pyridine ring [19].

In this study, we assigned signals in NMR spectra on the basis of $^1$H–$^{13}$C HSQC and HMBC heteronuclear correlation spectra. The $\underline{C}(NH_2)$ signal in the spectrum of compound **VII** has a value of 152.8 ppm, characteristic of tautomer **D** (149.3–154.6 ppm [15]) and close to the corresponding signal (152.1 ppm) in a synthesized model compound, 5-amino-3-phenyl-1,2,4-triazole (**XVI**), in which the proton of the acid can only be added to the N atom of the triazole ring.

The fact that the signals from the C-6' atom of the pyridine ring in compound **VII** and tautomer **A** of compound **I** are close (149.1 and 149.2 ppm [10], respectively) indicates that the nitrogen in the pyridine ring in salt **VII** is not protonated. In compound **IX**, the $\underline{C}(NH_2)$ signal is observed at 157.8 ppm, a value that is characteristic of tautomer **A** of C-amino-1,2,4-triazoles [10, 15] and is very close to the corresponding signal in tautomer **A** of compound **III** (157.6 ppm [10]).

The signal from C-2' and C-6' atoms (142.9 ppm) of the pyridine ring is substantially shifted upfield, compared with the corresponding signal in compound **III**, 149.9 ppm. This means that the nitrogen of the pyridine ring in salt **IX** is protonated. In compound **VIII**, the $\underline{C}(NH_2)$ signal has an intermediate value (154.8 ppm) for tautomers **A** and **D**, which presumably indicates that both tautomers are present and their signals coalesce [20].

The signals from C-2' (142.9 ppm) and C-6' atoms (146.6 ppm) are somewhat shifted upfield relative to the spectrum of the unprotonated compound **II**), 146.5 and 149.0 ppm, respectively [10]. This is also indicative of the presence of a tautomer in which the proton is bonded to the N atom of the pyridine moiety.

Taking into account published data [10, 15] and the chemical shifts in the spectrum of compound **XVI**, we can tentatively assume that the chemical shift of $\underline{C}(NH_2)$ is 152.1 ppm for tautomers **D** and 157.8 ppm for tautomers **A**. Then, using the extrapolation method [20], we can

estimate the content of tautomers of compound **VIII** in solution, which constitutes about 47% tautomer **A** and 53% tautomer **D**. Thus, compound **VII** is mostly present in a solution in DMSO as a tautomer **D**; compound **IX**, as tautomer **A**; and compound **VIII**, as a mixture of tautomers **A** and **D** in approximately equal amounts.

To find the place of proton addition in salts **VII–XIX** in an aqueous solution, we determined $pK_{BH^+}$ of triazoles **I–III** and of the model compound, 5-amino-1-phenyl-1,2,4-triazole (**XVII**). Compounds **I** and **XVII** have very close $pK_{BH^+}$ values of 3.82 ± 0.04 and 3.80 ± 0.03, respectively. This indicates that proton addition occurs at the same place and cations of the same type appear in the tautomeric form **D** [21]. The $pK_{BH^+}$ value for compound **III**, 4.68 ± 0.05, substantially exceeds that for compounds **I** and **XVII** and most of C-amino-1,2,4-triazoles [21]. It is reasonable to suggest that, in water, as also in DMSO, the cation of salt **IX** is predominantly in the tautomeric form **A**, i.e., the proton is bonded to the N atom of the pyridine ring. This structure was unambiguously confirmed by X-ray diffraction analysis of a crystal hydrate of compound **IX** [17]. Compound **II** has an average $pK_{BH^+}$ value of 4.05 ± 0.04. Presumably, two tautomers, **A** and **D**, are present in the aqueous solution of salt **VIII**.

## EXPERIMENTAL

We used aminoguanidine hydrocarbonate with the main substance content of not less than 98% (Merck), acids **X–XII** with the main substance content of not less than 99% (Acros Organics), and the rest of the reagents of chemically pure grade. Guanyl hydrazides **IV–VI**, necessary for determining the extinction coefficients of compounds **XIII–XV**, and compound **XVI** were produced using the known methods [2, 7, 8]. The NMR spectra were recorded on a Bruker Avance 600 spectrometer (600 MHz for $^1H$ and 150 MHz for $^{13}C$, solvent DMSO-$d_6$, internal standard TMS), and mass spectra, on a Finnigan MAT Incos 50 instrument with direct introduction of a sample into the ion emission source with an ionization energy of 70 eV. The spectrophotometric analysis was made with a Shimadzu UV-1800 instrument. The elemental analysis was performed with a Perkin–Elmer 2400 analyzer. The melting points were determined in sealed capillaries on a PTP instrument. The acidity of solutions was determined on a Mettler Toledo S40-KS instrument with InLab®Expert Pro combined electrode. The temperature of reaction mixtures was maintained to within ±0.5° with a thermostat having the form of an oil bath placed on an IKA RCT heated basic magnetic rabble equipped with an external thermocouple.

The reaction between aminoguanidine and acid **XI** was performed in an aqueous solution at AG and acid **XI** concentrations of 0.6–1 and 0.3–0.5 M, respectively, by the procedure described in [12]. The rate constant $k'$ was found from the initial portions of kinetic curves (up to AG conversion of up to 10–15%), with the reaction reversibility neglected. At pH 0.50 ± 0.01, the reaction rate is satisfactorily described by the kinetic equation

$$\frac{dc_{AG}}{d\tau} = -k'c_{AG}c_{\mathbf{XI}},$$

where $k'$ is the effective rate constant, and $c_{AG}$ and $c$**XI** are the analytical concentrations of AG and acid **XI**, respectively, in the reaction mixture (M).

The AG concentration was found by iodometric titration [12].

The ionization constants $pK_{BH^+}$ of compounds **I–III** and **XVII** were determined by potentiometric titration of 0.01 M solutions of compounds **I–III** and **XVII** in water with a 0.1 N HCl solution at a temperature of 20 ± 0.1°C by the method described in [22].

**Effect of reaction conditions on the course of the reaction between AG and acids X–XII.** The experiments were performed in 15-ml open glass test tubes. The reaction mixture was agitated with a magnetic rabble. A 1.00-g portion (7.3 mmol) of aminoguanidine hydrocarbonate, 0.90 g of the corresponding pyridinecarboxylic acid (**X–XII**), and a required amount of a 33.5% aqueous solution of HCl were placed in each test tube. The test tubes were heated in a thermostat to a required temperature of the reaction mixture (with water evaporated in the process), kept at this temperature for a required time, and cooled. Then their contents were dissolved in 0.1 N HCl and the resulting solution was analyzed.

The concentrations of compounds **VII–IX** and **XIII–XV** were determined spectrophotometrically. For this purpose, the optical density of a sample solution in cuvettes was determined with a 1-cm-thick absorbing layer at an analytical wavelength λ (Table 2). As a reference solution served a 0.1 N HCl solution. The concentration of compounds **VII–IX** was calculated by

**Table 2.** Analytical wavelengths λ and extinction coefficients ε of the reaction mixture components in 0.1 N HCl

| R | λ, nm | $\varepsilon_{RCOOH}$ | $\varepsilon_{ГТ}$ | $\varepsilon_{AT}$ |
|---|---|---|---|---|
| Pyridin-2-yl | 306.6 | 34 | 108 | 7102 |
| Pyridin-3-yl | 280.0 | 114 | 428 | 6152 |
| Pyridin-4-yl | 300.0 | 70 | 231 | 6507 |

the formula

$$c_{AT} = \frac{A - \varepsilon_{RCOOH}c_{RCOOH} - \varepsilon_{GH}(c_{RCOOH_0} - c_{RCOOH})}{\varepsilon_{AT} - \varepsilon_{GH}},$$

where $c_{AT}$ is the concentration of the hydrochloride of the corresponding aminotriazole **VII**–**IX**; $c_{RCOOH}$ and $c_{RCOOH0}$, running and initial concentration of acids **X**–**XII**, respectively (M); $\varepsilon_{RCOOH}$, $\varepsilon_{GH}$, and $\varepsilon_{AT}$, extinction coefficients of acids **X–XII**, guanyl hydrazides **XIII**–**XV**, and aminotriazoles **VII**–**IX**, respectively (Table 2). The concentration $c_{RCOOH}$ was calculated by the formula

$$c_{RCOOH} = c_{RCOOH_0} - (c_{AG_0} - c_{AG}),$$

where $c_{AG0}$ is the initial concentration of aminoguanidine. By he initial concentrations $c_{RCOOH_0}$ and $c_{AG_0}$ are understood the concentrations that would be observed in a sample at a zero conversion of AG and pyridinecarboxylic acid.

The concentration of guanyl hydrazides, $c_{GH}$ (M), was calculated by the formula

$$c_{GH} = c_{RCOOH_0} - c_{RCOOH} - c_{AT.}$$

**5-Amino-3-(pyridin-2-yl)-1,2,4-triazole hydrochloride (VII).** A 5.53-g portion (0.0406 mol) of aminoguanidine hydrocarbonate was mixed with 5.01 g (0.0406 mol) of pyridine-2-carboxylic acid and 5.75 g (0.0528 mol) of a 33.5% HCl solution. The resulting mixture was heated under agitation to boiling, until its temperature reached 180–185°C. Then the reaction mixture was kept at 180–185°C for 6 h, cooled to approximately 100°C, and 5 ml of water was added. The resulting solution was cooled to 3–5°C, and the precipitate formed was filtered off, recrystallized from water, and dried at 130°C. Yield 6.26 g (78%), mp 248–250°C. $^1$H NMR spectrum, δ, ppm: 7.57 m (1H, H-5'), 7.80 br.s (2H, $NH_2$), 8.02 m (2H, H-3' and H-4'), 8.68 m (1H, H-6'). $^{13}$C NMR spectrum, δ, ppm: 121.17 (C-3'), 125.89 (C-5'), 138.56 (C-4'), 143.88 (C-2'), 148.62 (C-3), 149.10 (C-6'), 152.78 (C-5). Mass-spectrum, *m/z* ($I_{rel}$, %): 161 (32) $[M\text{-HCl}]^+$, 106 (44), 105 (100), 78 (49), 51 (29), 38 (16), 36 (34). Found by potentiometric titration: $M$ = 197.9. Calculated: $M$ = 197.62. Found (%): C 42.26, H 4.19, N 35.22. $C_7H_8ClN_5$. Calculated (%): C 42.54, H 4.08, N 35.44.

**5-Amino-3-(pyridin-3-yl)-1,2,4-triazole hydrochloride (VIII).** Obtained similarly to compound **VII**. Yield 6.42 g (80%), mp 236–238°C. $^1$H NMR spectrum, δ, ppm: 7.82 d.d (1H, H-5', 3J 8.1 and 5.2 Hz), 7.90 br.s (2H, $NH_2$), 8.59 d.t (1H, H-4', $^3J$ = 8.1 Hz, $^4J$ = 1.8 Hz), 8.80 d.d (1H, H-6', 3J = 5.2 Hz, $^4J$ = 1.4 Hz), 9.16 d (1H, H-2', $^4J$ = 2.0 Hz). $^{13}$C NMR spectrum, δ, ppm: 125.65 (C-5'), 126.01 (C-3'), 137.17 (C-4'), 142.89 (C-2'), 146.63 (C-6'), 149.82 (C-3), 154.83 (C-5). Mass-spectrum, *m/z* ($I_{rel}$, %): 161 (100) $[M\text{-HCl}]^+$, 119 (20), 105 (34), 78 (19), 57 (16), 51 (14), 36 (11). Found by potentiometric titration: $M$ = 197.3. Calculated: $M$ = 197.62. Found (%): C 42.33, H 3.95, N 35.27. $C_7H_8ClN_5$. Calculated (%): C 42.54, H 4.08, N 35.44.

**5-Amino-3-(pyridin-4-yl)-1,2,4-triazole hydrochloride (IX).** Obtained similarly to compound **VII**. Yield 5.94 g (74%), mp 305–307°C. $^1$H NMR spectrum, δ, ppm: 6.51 br.s (2H, $NH_2$), 8.28 d.d (2H, H-3' and H-5', $^3J$ = 5.3 Hz, $^4J$ = 1.4 Hz), 8.88 m (2H, H-2' and H-6', $^3J$ = 5.3 Hz, $^4J$ = 1.4 Hz). $^{13}$C NMR spectrum, δ, ppm: 121.78 (C-3' and C-5'), 142.92 (C-2' and C-6'), 145.51 (C-4'), 153.71 (C-3), 157.83 (C-5). Mass-spectrum, *m/z* ($I_{rel}$, %): 161 (100) $[M\text{-HCl}]^+$, 119 (20), 105 (25), 78 (19), 57 (20), 51 (16), 36 (14). Found by potentiometric titration: $M$ = 197.4. Calculated: M = 197.62. Found (%): C 42.31, H 4.27, N 35.19. $C_7H_8ClN_5$. Calculated (%): C 42.54, H 4.08, N 35.44.

**5-Amino-3-(pyridin-2-yl)-1,2,4-triazole (I).** A 5.53-g portion (0.406 mol) of aminoguanidine hydrocarbonate was mixed with 5.01 g (0.0406 mol) of pyridine-2-carboxylic acid and 5.75 g (0.0528 mol) of a 33.5% HCl solution. The resulting mixture was heated to boiling under agitation and water was gradually evaporated until the temperature of the reaction mixture reached a value of 180°C. Then the reaction mixture was kept at 180–185°C for 3 h, cooled to approximately 100°C, and a solution of 4.3 g (0.108 mol) of NaOH in 20 ml of water was added. The resulting mixture was boiled under agitation for 10 min, neutral-

ized with a 20% HCl solution to pH 8–9, and cooled to 3–5°C. The precipitate formed was filtered off, recrystallized from water, and dried at 130°C. Yield 5.0 g (76%), mp 216–217°C (mp 220–221°C [10]). $^1$H NMR spectrum, δ, ppm: 5.32 br.s (2H, $NH_2$ of tautomer B), 6.07 br.s (2H, $NH_2$ of tautomer **A**), 7.32–7.43 m (1H, H-5'), 7.81–7.90 m (2H, H-3' and H-4'), 8.57 m (1H, H-6'), 12.22 br.s (1H, NH of tautomer **A**), 13.44 br.s (1H, NH of tautomer **B**). Mass-spectrum, *m/z* ($I_{rel}$, %): 161 (45) $[M]^+$, 105 (100), 78 (40), 51 (24). Found by potentiometric titration: $M$ = 161.3. Calculated: $M$ = 161.16. Found (%): C 51.95, H 4.44, N 43.61. $C_7H_7N_5$. Calculated (%): C 52.17, H 4.38, N 43.45.

**5-Amino-3-(pyridin-3-yl)-1,2,4-triazole (II).** Obtained similarly to compound **I**. Yield 5.23 g (80%), mp 226–227°C (mp 224–225°C [10]). $^1$H NMR spectrum, δ, ppm: 6.15 br.s (2H, $NH_2$), 7.41 d.d (1H, H-5', $^3J$ 7.8 and 4.8 Hz), 8.16 d.t (1H, H-4', $^3J$ = 8.1 Hz, $^4J$ = 1.8 Hz), 8.53 d.d (1H, H-6', $^3J$ = 5.1 Hz, $^4J$ = 1.8 Hz), 9.03 d (1H, H-6', $^4J$ = 1.2 Hz), 12.28 br.s (1H, NH). Mass-spectrum, *m/z* ($I_{rel}$, %): 161 (100) $[M]^+$, 119 (20), 105 (32), 78 (14), 57 (11). Found by potentiometric titration: $M$ = 160.8. Calculated: $M$ = 161.16. Found (%): C 52.01, H 4.28, N 43.71. $C_7H_7N_5$. Calculated (%): C 52.17, H 4.38, N 43.45.

**5-Amino-3-(pyridin-4-yl)-1,2,4-triazole (III).** Obtained similarly to compound **I**. Yield 4.62 g (70%), mp 271–272°C (mp 272–274°C [10]). $^1$H NMR spectrum, δ, ppm: 6.22 br.s (2H, $NH_2$), 7.76 d.d (2H, H-3' and H-5', $^3J$ = 4.5 Hz, $^4J$ = 1.5 Hz), 8.57 d (2H, H-2' and H-6', $^3J$ = 5.7 Hz), 12.35 br.s (1H, NH). Mass-spectrum, *m/z* ($I_{rel}$, %): 161 (100) $[M]^+$, 119 (13), 105 (18), 78 (12), 57 (13), 51 (11). Found by potentiometric titration: $M$ = 161.4. Calculated: $M$ = 161.16. Found (%): C 52.26, H 4.35, N 43.39.

$C_7H_7N_5$. Calculated (%): C 52.17, H 4.38, N 43.45.

**5-Amino-3-phenyl-1,2,4-triazole hydrochloride (XVI).** To a solution of 1 g (6.2 mmol) of 5-amino-3-phenyl-1,2,4-triazole (**XVII**) in 5 ml of ethanol was added under agitation and heating to boiling a 0.74-g portion (6.8 mmol) of a 33.5% aqueous solution of HCl, the mixture was cooled to 0–5°C, and the precipitate formed was filtered off, recrystallized from ethanol, and dried at 130°C. Yield 0.79 g (65%), mp 258–260°C. $^1$H NMR spectrum, δ, ppm: 7.50 m (3H, Ph), 7.95 m (2H, Ph), 8.00 br.s (2H, $NH_2$). $^{13}$C NMR spectrum, δ, ppm: 124.99 (C-1'), 125.97 (C-2' and C-6'), 128.96 (C-3' and C-5'), 130.97 (C-4'), 148.57 (C-3), 152.07 (C-5). Mass-spectrum, *m/z* ($I_{rel}$, %): 160 (100) $[M\text{-HCl}]^+$, 118 (15), 104 (55), 77 (23), 57 (12). Found (%): C 49.05, H 4.65, N 28.58. $C_8H_9ClN_4$. Calculated (%): C 48.86, H 4.61, N 28.49.

## CONCLUSIONS

(1) 3-Pyridyl-substituted 5-amino-1,2,4-triazoles should be synthesized without isolation of guanyl hydrazides by heating a mixture of aminoguanidine hydrocarbonate, pyridinecarboxylic acid, and hydrochloric acid in a 1 : 1.3 : 1 molar ratio in the course of 5–6 h at a temperature of 180–185°C. When obtaining free aminotriazoles, it is advisable to diminish the duration of the acid-catalyzed stage of synthesis to 3 h and to cyclize guanyl hydrazides by boiling an aqueous-alkaline solution of the reaction mixture.

(2) The N-4 atom of the triazole ring is protonated in 5-amino-3-(pyridin-2-yl)-1,2,4-triazole hydrochloride, and the N-1' atom of the pyridine moiety, in 5-amino-3-(pyridin-4-yl)-1,2,4-triazole. In 5-amino-3-(pyridin-2-yl)-1,2,4-triazole hydrochloride solutions, both tautomers are present in comparable concentrations.

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