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Cyclotransformation in the Series of Fused 5-Nitropyridin-2(1*H*)-ones

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Abstract—Reactions with excess hydrazine hydrate of 5-nitropyridin-2(1*H*)-ones fused with benzene, pyridine, and 1,2,3-triazole rings led to a cyclotransformation of the 5-nitro-2-oxopyridine fragment into the 6-methyl-3-oxopyridazine structure. This cyclotransformation is of general character; a probable mechanism of the process is suggested. Details of the assumed mechanism were experimentally confirmed on model compounds.

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In the course of the study on the chemical properties of substituted 7-nitro-1,5-dihydro-4*H*-imidazo[4,5-*c*]-pyridin-4-ones we found that these compounds treated with excess hydrazine hydrate underwent a conversion into derivatives of 7-methyl-1,5-dihydro-4*H*-imidazo-[4,5-*d*]pyridazin-4-one [1].

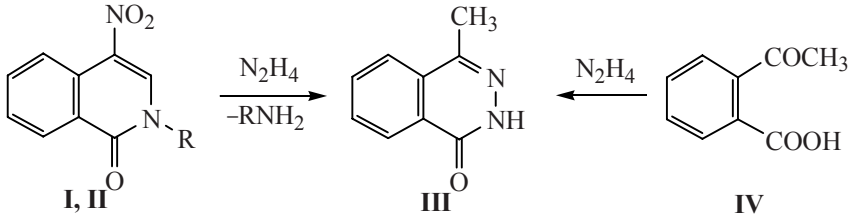
Therefore an interest was generated whether a similar transformation would occur also in the series of other fused heterocycles containing 5-nitro-2-oxopyridine fragment.

Actually, the heating of 4-nitroisoquinolin-1(2*H*)-one (**I**) and its N-methyl derivative **II** with hydrazine hydrate led to the formation of the same compound that based on the elemental analysis, IR and ^{1}H NMR spectra could be regarded as 4-methylphthalazin-1(2*H*)-one (**III**). Its ^{1}H NMR spectrum contains a singlet from the methyl group at 2.60 and a multiplet from the protons of the benzene ring in the region 7.92–8.23 ppm [2]. In the course of the cyclotransformation of nitroisoquinolines **I** and **II** a liberation of gaseous ammonia and methylamine occurred whose formation was proved by mass spectrometry. The validity of the assumed structure **III** [2] was proved by the lack of melting point depression in a mixed sample of compound **III** and 4-methylphthalazin-1(2*H*)-one independently synthesized [3] from 2-acetylbenzoic acid (**IV**), and by the coincidence of their IR and ^{1}H NMR spectra (Scheme 1).

Similarly to the above heterocycles **I** and **II** 6-methyl-8-nitro-1,6-naphthyridin-5(6*H*)-one (**V**) also underwent cyclotransformation giving 8-methylpyrido[2,3-*d*]pyridazin-5(6*H*)-one (**VI**), and the accompanying evolution of gaseous ammonia and methylamine was proved by mass spectrometry [4]. The composition and structure of base **VI** obtained was proved by its independent synthesis from 2-acetylnicotinic acid (**VII**) by procedure [5], by the data of elemental analysis, IR, and ^{1}H NMR spectra (Scheme 2).

Inasmuch as the 1,2,3-triazolo[4,5-*c*]pyridine was one of the closest 2-azaanalogs of imidazo[4,5-*c*]-pyridine it was rational to subject to the cyclotransformation 7-nitro-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*c*]pyridin-4-one (**VIII**) and its N^1-alkyl derivatives **IX–XIII**.

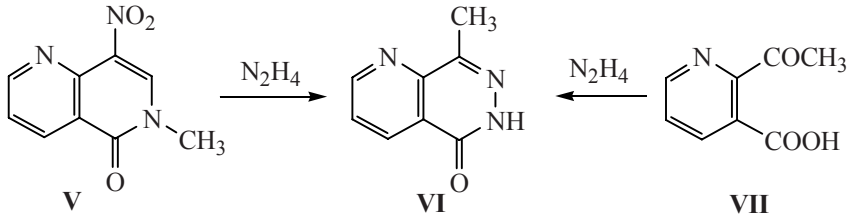
Scheme 1.



I, II **III** **IV**

† Deceased.

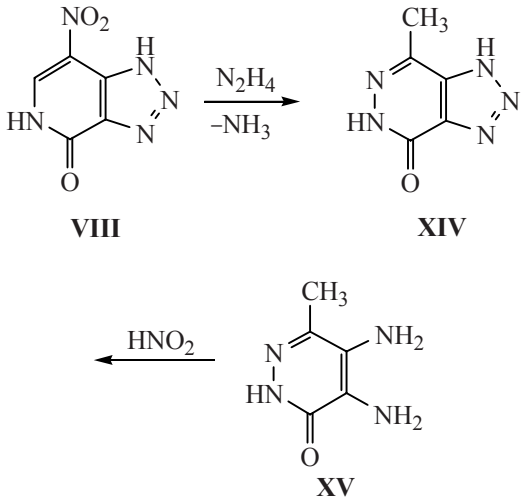
Scheme 2.



V **VI** **VII**

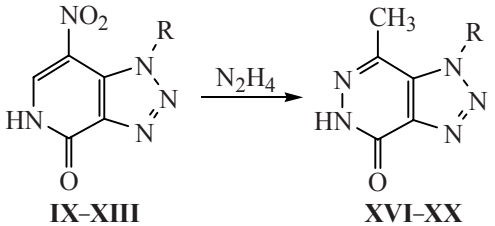
It turned out that a short heating of nitro compound **VIII** with hydrazine hydrate provided compound **XIV** in nearly quantitative yield. The ^{1}H NMR spectrum of the compound contained an only singlet signal at 2.90 ppm characteristic of the protons of the methyl group. These results indicate that the cyclotransformation occurs also in this case resulting in 7-methyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*d*]pyridazin-4-one (**XIV**). The identity of compound **XIV** obtained to an authentic sample synthesized from 4,5-diamino-6-methylpyridazin-3(2*H*)-one (**XV**) by procedure [6] confirmed the validity of the above conclusion (Scheme 3).

Scheme 3.



VIII **XIV** **XV**

Scheme 4.



IX–XIII **XVI–XX**

R = Me (**IX, XVI**), Et (**X, XVII**), Bu (**XI, XVIII**), $(CH_2)_3NMe_2$ (**XII, XIX**), cyclo-C_6H_{11} (**XIII, XX**).

In the same way as nitro compound **VIII** its N*1*-alkyl derivatives **IX–XIII** treated with hydrazine hydrate also suffered the cyclotransformation into 7-methyl-N*1*-alkyl-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*d*]pyridazin-4-ones **XVI–XX**.

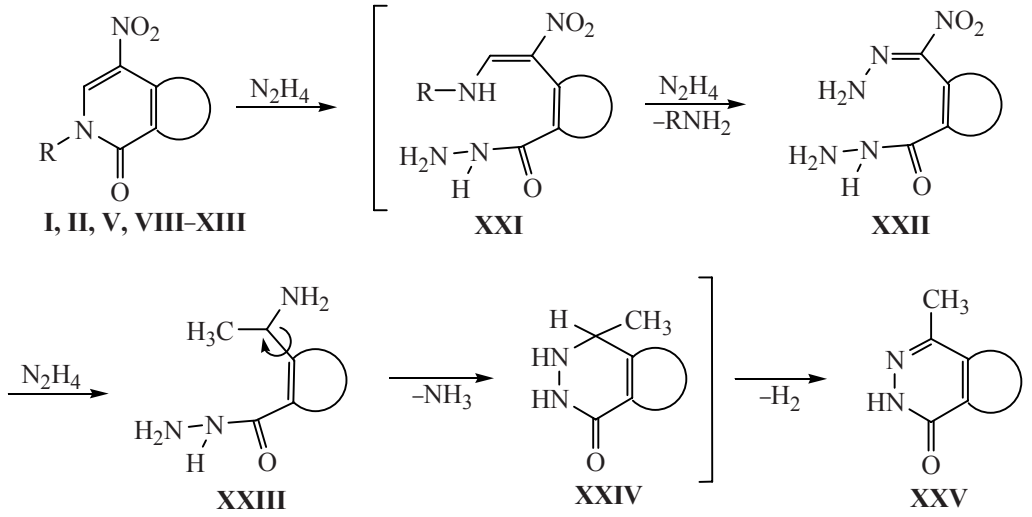
In the IR spectra of obtained compounds **XVI–XX** characteristic absorption bands $\nu_{C=O}$ were observed in the region 1685–1700 cm^{-1}. In the ^{1}H NMR spectra of compounds **XVI–XX** signals were present from the C-methyl groups in the pyridazine ring with the chemical shifts 2.74–2.85 ppm, and also the signals of the N*1*-alkyl groups.

We showed by examples of fused heterocycles **I, II, V**, and **VIII–XIII** containing a fragment of 5-nitropyridin-2(1*H*)-one that the described type of cyclotransformation into pyridazinone derivatives was of a general character, and we suggested a mechanism of the process.

The details of the assumed mechanism were confirmed experimentally on model compounds. The fact that the cyclotransformation of fused nitropyridones **I, II, V**, and **VIII–XIII** cannot start by reduction of the nitro group is proved by the lack of reaction between the hydrazine hydrate and 4-aminoisoquinolin-1(2*H*)-one (**XXVI**) or 7-amino-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*c*]pyridin-4-one (**XXVII**).

The opportunity of the cyclotransformation originates from the electron-withdrawing effect of the nitro group on the carbonyl carbon of the pyridine fragment in the initial compounds thus permitting the nucleophilic attack of the hydrazine on this carbon atom resulting in the opening of the pyridine ring. The necessity of the nitro group presence in structures **I, II, V**, and **VIII–XIII** is proved by the lack of cyclotransformation in reaction with hydrazine hydrate of 1-methyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one (**XXVIII**) or its 7-bromo derivative **XXIX** (Scheme 5). The opening of the pyridine ring in compounds **I, II, V**, and **VIII–XIII** led to the formation of structure **XXI** containing a carbohydrazide group and aminoethylene moiety; the

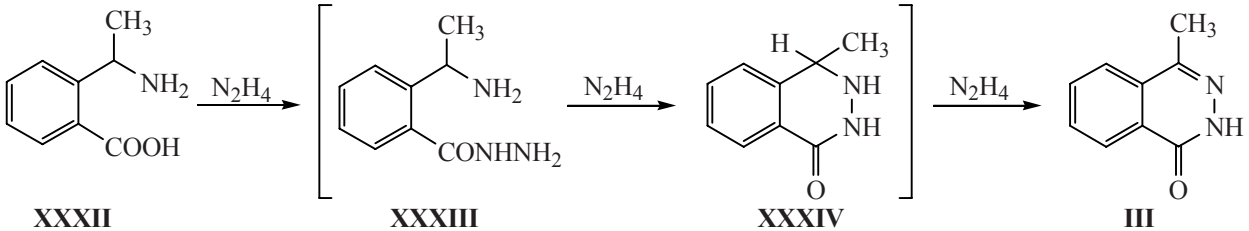
Scheme 5.



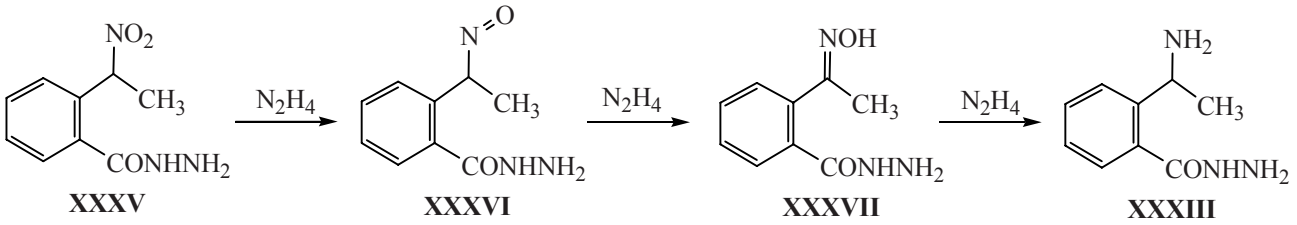
transformation of the latter govern further process according to the assumed scheme. We showed first of all that the methyl group in structure **XXIII** formed from hydrazone **XXII**. To this end initial compound **IX** was subjected to the cyclotransformation in excess of hydrazine-D_4 to obtain 7-dideuteromethyl-1-methyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*d*]pyridazin-4-one (**XXX**). In the ^{1}H NMR spectrum of compound **XXX** obtained the area under the peak of the C-methyl group is equal to 1/3 of the area under the signal of the N*1*-methyl group proving the formation of the dideuteromethyl group CHD_2. The formation of hydrazone **XXII** should involve evolution of, for instance, methylamine at treatment with hydrazine of nitro compounds **II** and **V**, or ammonia in reaction of compounds **I** and **VIII–XIII**. Thus the NH–R group at the nitroethylene fragment (structure **XXI**) gets replaced by hydrazino group (structure **XXII**). It was shown that the amino group of structure **XXIII** was liberated as NH_3 involving the terminal hydrogen of the hydrazide group, and this led to the formation of bicycle **XXIV**. The data of mass-spectroscopic measurements confirmed that among the gaseous products of hydrazine reaction with 1-methyl-7-nitro(^{15}N)-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*c*]pyridin-4-one (**XXXI**) ammonia $^{15}NH_3$ was present. This result demonstrates that in formation of the pyridazine ring both its nitrogens originate from the hydrazine. The actual formation and conversion of structures of the type **XXIII, XXIV** into the final methylpyridazinone **XXV** was supported by heating the hydrazine hydrate with 2-α-aminoethylbenzoic acid (**XXXII**) to obtain in nearly quantitative yield phthalazone **III** [7] through the stages of formation of hydrazide **XXXIII** and dihydrophthalazone **XXXIV** (Scheme 6).

In this connection it was presumable that 2-α-aminoethylbenzoic acid hydrazide **XXXIII** is the reduction product of α-nitroethylbenzoic acid hydrazide **XXXV** formed in reaction with hydrazine of 4-nitroquinolin-1(2*H*)-one (**I**). It is quite possible that these transformations occurring in the side chain of the α-nitroethyl fragment are related to the reduction by the hydrazine of the nitro group to nitroso group (**XXXVI**),

Scheme 6.



Scheme 7.



and the isomerization of the latter may result in 2-acetylbenzoic acid oxime (**XXXVII**) followed by its further reduction into amino derivative **XXXIII**.

To prove this assumption we brought into the reaction with hydrazine a model compound, 2-acetylbenzoic acid oxime (**XXXVII**). It turned out that in conditions analogous to used with amino compound **XXXII** oxime **XXXVII** reacted with hydrazine giving in nearly quantitative yield also 4-methylphthalazin-1(2*H*)-one (**III**).

The described cyclotransformation of fused 5-nitropyridin-2(1*H*)-ones **I, II, V**, and **VIII–XIII** results from a series of successive transformations whose specificity and consistency is evidenced by the high purity and yields (up to 99%) of fused pyridazinones. A significant feature of this reaction consists in the driving from the pyridine ring of the initial nitro compound in the course of pyridazine ring formation of one methine group (6-CH) and its reduction to methyl. A necessary condition for the cyclotransformation reaction to occur is the presence of an α-carbonyl group and a nitro group in the position *5* of the pyridine ring fused to an aromatic ring [8].

EXPERIMENTAL

^{1}H NMR spectra were registered on a spectrometer Tesla BS-467 at operating frequency 80 MHz from solution in CF_3COOH, and also on a spectrometer Varian Gemini-200 at operating frequency 200 MHz from solutions in CD_3OD, DMSO-d_6, and DMF-d_7, internal reference HMDS.

IR spectra of compounds synthesized were recorded on spectrophotometers UR-20 and Specord 75IR from samples pelletized with KBr or in mulls with mineral oil.

Molecular mass of compounds was measured by mass spectrometry on Varian MAT-112 instrument with direct admission of a sample into the ion source at the energy of ionizing electrons 70 eV.

The purity and homogeneity of compounds obtained was checked by TLC on Silufol UV-254 plates (eluent ethanol, detection in iodine vapor and under UV irradiation). Synthesis of compounds **I** and **II** is described in [9], compound **XI** was prepared by procedure [10].

4-Methylphthalazin-1(2*H*)-one (III). *a.* A solution of 0.6 g (3.15 mmol) of 4-nitroisoquinolin-1(2*H*)-one (**I**) in 3.0 ml (64.2 mmol) of hydrazine hydrate was heated for 3–5 h at 130–140°C. On dissolution of compound **I** in the hydrazine hydrate the solution got dark red. In the course of the reaction ammonia liberated that was passed through an ethanol solution of hydrogen chloride and then identified as ammonium chloride (mp 334–336°C). To the end of the reaction the solution decolorized. Then the hydrazine hydrate was distilled off in a vacuum of a water-jet pump. To the residue 5.0 ml of 2-propanol was added, and the reaction product was filtered off. Yield 0.4 g (80%), mp 220–222°C (ethanol) (221–222°C [3]). IR spectrum, ν, cm^{-1}: 1670 (C=O). ^{1}H NMR spectrum (CF_3COOH), δ, ppm: 7.92–8.23 m (4H, C_6H_4). Found, %: C 67.36; H 4.96; N 17.37. $C_9H_8N_2O$. Calculated, %: C 67.49; H 5.03; N 17.49.

b. The synthesis was carried out similarly from 1.3 g (6.4 mmol) of 2-methyl-4-nitroisoquinolin-1(2*H*)-one (**II**) and 6.5 ml (130 mmol) of hydrazine hydrate. In the course of the reaction ammonia and methylamine liberated that were passed through an ethanol solution of hydrogen chloride and then identified as the corresponding hydrochlorides. Along with ammonium chloride {mp 332°C (336°C [11])} equimolar amount of methylamine hydrochloride was isolated with mp 224°C (226°C [11]). Hydrochlorides of ammonia and methylamine were separated due to their different solubility in anhydrous ethanol [12]. Methylamine was identified in the gas phase by mass spectrometry by its molecular ion peak (M^+ 31). Yield 0.61 g (60%), mp 219–221°C (ethanol) (221–222°C [3]). IR spectrum, ν, cm^{-1}: 1670 (C=O). ^{1}H NMR spectrum (CF_3COOH), δ, ppm: 2.60 s (3H, 4-CH_3), 7.92–8.23 m (4H, C_6H_4). Found, %: C 67.33; H 4.97; N 17.35. $C_9H_8N_2O$. Calculated, %: C 67.49; H 5.03; N 17.49.

c. To a solution of 1.64 g (10.0 mmol) of *o*-acetylbenzoic acid (**IV**) in 10.0 ml of 1-PrOH was added

0.6 ml (12.8 mmol) of hydrazine hydrate, and the mixture was heated on a boiling water bath for 2 h. On cooling the separated white precipitate was filtered off and dried. Yield 1.3 g (87%), mp 220–222°C (ethanol). IR spectrum, ν, cm^{-1}: 1670 (C=O). ^1H NMR spectrum (CF_3COOH), δ, ppm: 2.60 s (3H, 4-CH_3), 7.91–8.23 m (4H, C_6H_4).

d. A mixture of 0.8 g (5 mmol) of 2-α-aminoethylbenzoic acid (**XXXII**) prepared by procedure [13], and 5 ml (100 mmol) of hydrazine hydrate was heated at 130–140°C for 4–5 h, then excess hydrazine hydrate was distilled off in a vacuum to dryness, the residue was ground with 3 ml of 2-propanol, and the precipitate was filtered off. Yield 0.78 g (quantitative), mp 222–224°C. IR spectrum, ν, cm^{-1}: 1670 (C=O). ^1H NMR spectrum (CF_3COOH), δ, ppm: 2.60 s (3H, 4-CH_3), 7.90–8.21 m (4H, C_6H_4). Found, %: C 67.35; H 4.99; N 17.38. $C_9H_8N_2O$. Calculated, %: C 67.49; H 5.03; N 17.49.

e. A mixture of 0.9 g (5 mmol) of 2-acetylbenzoic acid oxime (**XXXVII**) [14] and 5 ml (100 mmol) of hydrazine hydrate was heated at 135–140°C for 3–4 h, then excess hydrazine hydrate was distilled off in a vacuum to dryness, the residue was ground with 3 ml of 2-propanol, and the precipitate was filtered off. Yield 0.8 g (quantitative), mp 222–224°C (ethanol). IR spectrum, ν, cm^{-1}: 1670 (C=O). ^1H (CF_3COOH), δ, ppm: 2.59 s (3H, 4-CH_3), 7.93–8.22 m (4H, C_6H_4). Found, %: C 67.39; H 4.98; N 17.37. $C_9H_8N_2O$. Calculated, %: C 67.49; H 5.03; N 17.49.

6-Methyl-8-nitro-1,6-naphthyridin-5(6*H*)-one (V). To a solution of 0.8 g (5.0 mmol) of 6-methyl-5,6-dihydro-1,6-naphthyridin-5-one [15] in 12 ml of concn. H_2SO_4 was added within 0.5 h at 0–5°C a solution of 2.4 ml (57.4 mmol) of fuming nitric acid (*d* 1.5 g/cm^3) in 4 ml of concn. H_2SO_4. The reaction mixture was gradually warmed to 10°C and kept at that temperature for 0.5 h. Then the mixture was warmed to room temperature and in 1 h it was poured into ice water and neutralized with sodium carbonate. The solution was evaporated to dryness, and the reaction product was extracted from the residue into ethanol. Yield 0.88 g (86%), mp 200–201°C (benzene–heptane, 2:1). ^1H NMR spectrum (CF_3COOH), δ, ppm: 3.81 s (3H, N^6CH_3), 8.22 s (1H, H^7), 9.20–9.63 m (3H, H^{2-4}). Found, %: C 52.73; H 3.42; N 20.41. $C_9H_7N_3O_3$. Calculated, %: C 52.69; H 3.44; N 20.48.

8-Methylpyrido[2,3-*d*]pyridazin-5(6*H*)-one (VI) was obtained from 1.2 g (5.84 mmol) of reagent **V** and 6.0 ml (128.4 mmol) of hydrazine hydrate in the same way as compound **III** (method *b*). In the course of the reaction evolved methylamine, that was passed through an alcoholic solution of picric acid and then identified as picrate {mp 214–216°C (215°C [16])}, and also by its molecular ion peak in the mass spectrum of the gas phase (M^+ 31). Yield 0.74 g (94%), mp 249–250°C (ethanol) (249–250°C [5]). IR spectrum, ν, cm^{-1}: 1700 (C=O). ^1H NMR spectrum (CF_3COOH), δ, ppm: 2.83 s (3H, 8-CH_3), 8.33–9.65 m (3H, H^2, H^3, H^4). Found, %: C 59.44; H 4.30; N 25.92. $C_8H_7N_3O$. Calculated, %: C 59.62; H 4.38; N 26.07.

7-Nitro-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]-pyridin-4-one (VIII). In 35 ml of concn. H_2SO_4 was dissolved 4.0 g (30.5 mmol) of 1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one [17] at stirring and cooling, then at 0–5°C was added dropwise 6 ml (144.7 mmol) of fuming nitric acid (*d* 1.5 g/cm^3), and the reaction mixture was maintained at this temperature for 0.5–1.0 h. The reaction mixture was gradually warmed to room temperature, heated for 2–3 h at 60°C, cooled, poured on ice, and neutralized with ammonium hydrogen carbonate. The separated light-yellow precipitate was filtered off, washed with ethanol, with ether, and crystallized from water. Yield 3.0 g (54%), mp > 280°C (decomp.). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 8.43 s (1H, H^6). Found, %: C 33.25; H 1.74; N 38.70. $C_5H_3N_5O_3$. Calculated, %: C 33.16; H 1.67; N 38.67.

1-Methyl-7-nitro-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*c*]pyridin-4-one (IX). In 20 ml of concn. H_2SO_4 was dissolved 2.4 g (16.0 mmol) of 1-methyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one at stirring and cooling, then at 5–10°C was added by portions 2.4 g (22.0 mmol) of potassium nitrate, and the mixture was kept at this temperature for 0.5 h. The reaction mixture was gradually warmed to room temperature, heated for 2 h at 60°C, cooled, poured on ice, and neutralized with aqueous ammonia. The separated precipitate was filtered off, washed with ice water, and dried. Yield 2.0 g (75%), mp 278–281°C. ^1H NMR spectrum (CF_3COOH), δ, ppm: 4.60 s (3H, N^1CH_3), 8.83 s (1H, H^6). Found, %: C 36.85; H 2.61; N 35.94. $C_6H_5N_5O_3$. Calculated, %: C 36.93; H 2.58; N 35.89.

1-Methyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]-pyridin-4-one was obtained by procedure [17] from 4-chloro-1-methyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*C*]pyridine [18]. Yield 96%, mp 326–329°C (ethanol). IR spectrum, ν, cm^{-1}: 1670–1690 (C=O). ^1H NMR spectrum (CF_3COOH), δ, ppm: 4.52 s (3H, N^1CH_3), 7.20 d (1H, H^7, *J* 7.0 Hz), 7.82 d (1H, H^6, *J* 7.0 Hz). Found, %: C 47.79; H 3.94; N 37.14. $C_6H_6N_4O$. Calculated, %: C 48.00; H 4.00; N 37.3.

1-Ethyl-7-nitro-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*c*]pyridin-4-one (X) was obtained similarly to compound **IX** from 1.08 g (6.6 mmol) 1-ethyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one and 1.6 ml (38 mmol) of concn. HNO_3 (*d* 1.5 g/cm^3). Yield 1.0 g (73%), mp 212–214°C. ^{1}H NMR spectrum (CF_3COOH), δ, ppm: 1.21 t (3H, CH_2CH_3), 4.71 q (2H, CH_2CH_3), 8.45 s (1H, H^6). Found, %: C 40.05; H 3.30; N 33.32. $C_7H_7N_5O_3$. Calculated, %: C 40.20; H 3.37; N 33.48.

1-Ethyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]-pyridin-4-one was obtained by procedure [17] from 4-chloro-1-ethyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]-pyridine [18]. Yield 93%, mp 220–222°C. IR spectrum, ν, cm^{-1}: 1680–1690 (C=O). ^{1}H NMR spectrum (CF_3COOH), δ, ppm: 1.31 t (3H, CH_2CH_3), 4.43 q (2H, CH_2CH_3), 6.70 d (1H, H^7, *J* 7.0 Hz), 7.40 d (1H, H^6, *J* 7.0 Hz). Found, %: C 51.07; H 4.83; N 34.15. $C_7H_8N_4O$. Calculated, %: C 51.21; H 4.91; N 34.27.

1-Butyl-7-nitro-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*c*]pyridin-4-one (XI). To a solution of 0.8 g (4.2 mmol) of 1-butyl-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*c*]pyridin-4-one [10] in 8.0 ml of concn. H_2SO_4 was added by portions at 0°C a solution of 2.0 ml (48.0 mmol) of concn. HNO_3 (*d* 1.5 g/cm^3) in 2 ml of concn. H_2SO_4. After 0.5 h the mixture was warmed to 10°C and was kept at this temperature for 15 min. Then the reaction mixture was poured on 40 g of crushed ice, the separated precipitate was filtered off, washed with ice water, and dried. Yield 1.0 g (99%), mp 198–200°C. ^{1}H NMR spectrum (CF_3COOH), δ, ppm: 1.00 s (3H, δ-CH_3), 1.42 q (2H, γ-CH_2), 1.88 q (2H, β-CH_2), 5.10 t (2H, N$^1CH_2$), 8.88 s (1H, H^6). Found, %: C 45.39; H 4.61; N 29.38. $C_9H_{11}N_5O_3$. Calculated, %: C 45.57; H 4.67; N 29.52.

7-Nitro-1-(γ-*N,N*-dimethylaminopropyl)-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one (XII) was obtained similarly to compound **XI** from 1.5 g (5.8 mmol) of 1-(γ-*N,N*-dimethylaminopropyl)-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one hydrochloride and 1.4 ml (33.8 mmol) of concn. HNO_3 (*d* 1.5 g/cm^3). Yield 0.8 g (52%), mp 99–101°C (2-propanol). ^{1}H NMR spectrum (CF_3COOH), δ, ppm: 2.73 t (2H, γ-CH_2), 3.10 d [6H, N(CH_3)$_2$], 3.55 q (2H, β-CH_2), 5.22 t (2H, N$^1CH_2$), 8.93 s (1H, H^6). Found, %: C 45.00; H 5.25; N 31.40. $C_{10}H_{14}N_6O_3$. Calculated, %: C 45.11; H 5.30; N 31.56.

1-(γ-*N,N*-Dimethylaminopropyl)-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one hydrochloride was obtained by procedure [17] from 4-chloro-1-(γ-*N,N*-dimethylaminopropyl)-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*c*]pyridine [18]. Yield 93%, mp 246–249°C (ethanol). ^{1}H NMR spectrum (CF_3COOH), δ, ppm: 2.73 t (2H, γ-CH_2), 3.08 s [6H, N(CH_3)$_2$], 3.56 t (2H, β-CH_2), 4.90 t (2H, N$^1CH_2$), 7.18 d (1H, H^7, *J* 7.0 Hz), 7.78 d (1H, H^6, *J* 7.0 Hz). Found, %: C 46.41; H 6.20; N 26.98. $C_{10}H_{15}N_5$·HCl. Calculated, %: C 46.60; H 6.26; N 27.17.

7-Nitro-1-cyclohexyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one (XIII) was obtained similarly to compound **XI** from 0.45 g (2.1 mmol) of 1-cyclohexyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]-pyridin-4-one and 1.0 ml (24 mmol) of concn. HNO_3 (*d* 1.5 g/cm^3). Yield 0.52 g (98%), mp 228–231°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.27–2.25 m (10H, 5-CH_2), 4.93–5.15 m (1H, CH), 8.64 (1H, H^6). Found, %: C 50.02; H 4.94; N 26.46. $C_{11}H_{13}N_5O_3$. Calculated, %: C 50.19; H 4.98; N 26.60.

1-Cyclohexyl-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*c*]pyridin-4-one was obtained by procedure [17] from 4-chloro-1-cyclohexyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridine [18]. Yield 90%, mp 273–275°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.33–2.08 m (10H, 5-CH_2), 4.62–4.78 m (1H, CH), 6.82 d (1H, H^7, *J* 6.0 Hz), 7.37 d (1H, H^6, *J* 6.0 Hz). Found, %: C 60.41; H 6.39; N 25.52. $C_{11}H_{14}N_4O$. Calculated, %: C 60.53; H 6.46; N 25.67.

7-Methyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*d*]-pyridazin-4-one (XIV). A mixture of 0.8 g (4.4 mmol) of reagent **VIII** and 4.5 ml (90 mmol)of hydrazine hydrate was heated for 3–5 h at 135–140°C. In the course of the reaction ammonia liberated. On completion of the reaction excess hydrazine hydrate was distilled off in a vacuum till dryness, the residue was ground with 3 ml of 2-propanol, and the precipitate was filtered off. Yield 0.57 g (86%), mp 283–285°C (ethanol) [6]. IR spectrum, ν, cm^{-1}: 1680 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.90 s (3H, 7-CH_3). Found, %: C 39.65; H 3.36; N 46.42. $C_5H_5N_5O$. Calculated, %: C 39.74; H 3.33; N 46.34.

1,7-Dimethyl-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*d*]pyridazin-4-one (XVI). *a*. In 8.2 ml (175.5 mmol) of hydrazine hydrate was dissolved 1.7 g (8.7 mmol) of reagent **IX**, and the reaction was carried out similarly to the preparation of compound **XIV**. Yield 1.3 g (90%), mp 269–271°C (ethanol). IR spectrum, ν, cm^{-1}: 1690 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.86 s (3H, 7-CH_3), 4.56 s (3H, N$^1CH_3$). Found, %: C 43.45; H 4.22; N 42.28. $C_6H_7N_5O$. Calculated, %: C 43.64; H 4.27; N 42.40.

b. In 7.2 ml (154.1 mmol) of hydrazine hydrate was dissolved 1.5 g (7.6 mmol) of 1-methyl-7-nitro-(^{15}N)-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one (**XXXI**), and the reaction was carried out similarly to the preparation of compound **XIV**. In the course of the reaction gas evolution was observed. In order to identify the gas it was passed with an argon flow through a trap with concn. HCl. The hydrochloric solution was evaporated to dryness, the residue was ground with 2-propanol, and the product was filtered off like colorless crystals of mp 334°C. The mass of the product was measured by mass spectrometry to find molecular ion peaks M^+ 53 and M^+ 54 corresponding to ammonium chloride containing isotopes (^{14}N) and (^{15}N). The other part of the evolved gas under the pressure of the argon flow was placed into the trap for gas sampling. When the trap was completely filled with the gas it was introduced through an adapter into the mass spectrometer in order to measure the mass of the gaseous substance. The masses of the corresponding molecular ions were M^+ 17 and M^+ 18. Therefore the gas evolved was a mixture of $^{14}NH_3$ and $^{15}NH_3$. Yield of compound **XVI** 1.2 g (95%), mp 268–270°C (ethanol). IR spectrum, ν, cm^{-1}: 1690 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.85 s (3H, 7-CH_3), 4.56 s (3H, N^1CH_3). Found, %: C 43.47; H 4.23; N 42.25. $C_6H_7N_5O$. Calculated, %: C 43.64; H 4.27; N 42.40.

7-Methyl-1-ethyl-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*d*]pyridazin-4-one (XVII) was obtained from 0.9 g (4.2 mmol) of reagent **X** and 9 ml (180 mmol) of hydrazine hydrate similarly to compound **XVI**. Yield 0.75 g (97%), mp 181–183°C (2-propanol). IR spectrum, ν, cm^{-1}: 1700 (C=O). ^{1}H NMR spectrum (CD_3OD), δ, ppm: 1.70 t (3H, CH_2CH_3), 2.76 s (3H, 7-CH_3), 4.86 q (2H, CH_2CH_3). Found, %: C 46.79; H 5.01; N 38.93. $C_7H_9N_5O$. Calculated, %: C 46.92; H 5.06; N 39.09.

1-Butyl-7-methyl-1,5-dihydro-4*H*-1,2,3-triazolo-[4,5-*d*]pyridazin-4-one (XVIII) was obtained from 0.9 g (3.8 mmol) of reagent **XI** and 4.0 ml (80 mmol) of hydrazine hydrate similarly to compound **XVI**. Yield 0.72 g (92%), mp 151–153°C (ethanol). IR spectrum, ν, cm^{-1}: 1700 (C=O). ^{1}H NMR spectrum (CF_3COOH), δ, ppm: 0.97 t (2H, δ-CH_3), 1.49 q (2H, γ-CH_2), 2.85 s (2H, 7-CH_3), 4.90 q (2H, β-CH_2), 5.30 t (2H, α-CH_2). Found, %: C 52.05; H 6.30; N 33.71. $C_9H_{13}N_5O$. Calculated, %: C 52.16; H 6.32; N 33.80.

1-(γ-*N*,*N*-Dimethylaminopropyl)-7-methyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*d*]pyridazin-4-one hydrochloride (XIX) was obtained from 1.1 g (4.1 mmol) of reagent **XII** and 4.5 ml (90 mmol) of hydrazine hydrate similarly to compound **XVI**. Yield 0.91 g (93%). The reaction product was an oily base that was identified as hydrochloride. The alcoholic solution of the base was mixed with an ethanol solution of hydrogen chloride, and the separated precipitate was filtered off. mp >250°C (ethanol). IR spectrum, ν, cm^{-1}: 1685 (C=O). ^{1}H NMR spectrum (DMF-d_7), δ, ppm: 1.25 t (2H, γ-CH_2), 2.83 s (3H, 7-CH_3), 3.10 s [6H, N(CH_3)$_2$], 3.55 t (2H, β-CH_2), 3.95 t (2H, α-CH_2). Found, %: C 43.89; H 6.22; N 30.64. $C_{10}H_{16}N_6O$·HCl. Calculated, %: C 44.04; H 6.28; N 30.81.

7-Methyl-1-cyclohexyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*d*]pyridazin-4-one (XX) was obtained from 1.0 g (4.0 mmol) of reagent **XIII** and 9 ml (180 mmol) of hydrazine hydrate similarly to compound **XVI**. Yield 0.85 g (96%), mp 187–189°C (H_2O). ^{1}H NMR spectrum (DMF-d_7), δ, ppm: 1.28–2.38 m (10H, 5CH_2), 2.74 s (3H, 7-CH_3), 4.85–5.15 m (1H, CH). IR spectrum, ν, cm^{-1}: 1700 (C=O). Found, %: C 56.47; H 6.41; N 29.86. $C_{11}H_{15}N_5O$. Calculated, %: C 56.64; H 6.48; N 30.02.

7-Dideuteromethyl-1-methyl-1,5-dihydro-4*H*-triazolo[4,5-*d*]pyridazin-4-one (XXX) was obtained similarly to compound **XVI** from 1.0 g (5.1 mmol) of reagent **IX** and 5.7 ml (102 mmol) of deuterohydrazine hydrate ($N_2D_4 \cdot D_2O$). On completion of the reaction the deuterohydrazine hydrate was distilled off in an argon flow till dryness, the residue was ground with 1.0 ml of deuterium oxide, and the white precipitate was distilled off, dried, and recrystallized from dioxane to obtain colorless crystals. Yield 0.75 g (87%), mp 260–263°C. IR spectrum, ν, cm^{-1}: 1685 (C=O). ^{1}H NMR spectrum (DMSO-d-$_6$), δ, ppm: 2.03 s (1H, 7-CHD_2), 3.38 s (3H, N^1CH_3-). Found, %: C 42.69; H (D) 5.91; N 41.50. $C_6H_4N_5O$. Calculated, %: C 42.85; H (D) 5.99; N 41.64.

1-Methyl-7-nitro(^{15}N)-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one (XXXI). To a solution of 3.1 g (20.6 mmol) of 1-methyl-1,5-dihydro-4*H*-1,2,3-triazolo[4,5-*c*]pyridin-4-one in 25 ml of concn. H_2SO_4 at 0–5°C was added by portions 2.4 g (23.5 mmol) of dry K$^{15}NO_3$, and the reaction mixture was maintained at 0–5°C for 0.5–1.0 h. Then the reaction mixture was treated and worked up as described for compound **IX**. Yield 2.8 g (70%), mp 291–294°C (DMF). ^{1}H NMR spectrum (CF_3COOH), δ, ppm: 4.66 s (3H, N^1CH_3), 8.90 s (1H, H^6). Found, %: C 36.60; H 2.54; N 36.33. M^+ 196. $C_6H_5N_5O_3$. Calculated, %: C 36.74; H 2.57; N 36.22.

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