Substituted 3- and 5-formylpyridin-2-ones in the synthesis of 1-aryl-1,6-naphthyridinone derivatives

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New 1-aryl-6-[2-(dimethylamino)vinyl]-4-oxo-1,4-dihydropyrimidine-5-carbonitriles and 4-arylamino-2-oxo-1,2-dihydropyridine-3-carbonitriles containing electron-withdrawing substituents in the benzene ring were synthesized from enamino amides and dimethylformamide dialkylacetals. The influence of various dimethylformamide acetals on the yield of 3-(4-chloroanilino)-2-cyano-5-(dimethylamino)penta-2,4-dienoic acid *N*-(dimethylamino)methylideneamide was investigated in the reaction of these acetals with 3-(4-chloroanilino)-2-cyanocrotonamide. New 4-arylamino-5-formyl-2-oxo-1,2-dihydropyridine-3-carbonitriles and 4-arylamino-2-oxo-1,2-dihydropyridine-3-carbaldehydes containing electron-withdrawing substituents in the benzene ring were synthesized. The latter compounds were converted into new substituted 1,6-naphthyridinones by the action of various CH acids. A new approach to the synthesis of 4-(4-fluoroanilino)-5-formyl-2-oxo-1,2-dihydropyridine-3-carbonitrile using dimethylformamide diisopropylacetal under mild conditions was developed. The comparative reactivity of the formyl group in the reactions of 4-arylamino-5-formyl-2-oxo-1,2-dihydropyridine-3-carbonitriles and in 4-arylamino-2-oxo-1,2-dihydropyridine-3-carbaldehydes with malononitrile was determined using HPLC.

Key words: enamino amides, dimethylformamide acetals, 4-arylamino-2-oxo-1,2-dihydropyridine-3-carbonitriles, 3-arylamino-2-cyano-5-dimethylamino-*N*-[(dimethylamino)methylidene]penta-2,4-dien amides, 4-arylamino-5-formyl-2-oxo-1,2-dihydropyridine-3-carbonitriles, 4-arylamino-2-oxo-1,2-dihydropyridine-3-carbaldehydes, 1-aryl-3,8-dicyano-2-imino-1,6-naphthyridine-2,5(1*H*,6*H*)-diones, 1-aryl-5-chloro-3-nitro-1,6-naphthyridine-2(1*H*)-ones, the Knoevenagel reaction, X-ray diffraction, HPLC.

Enamines are important compounds usable in various fields of organic and medicinal chemistry. A number of reviews is devoted to their properties.[1,2] Numerous methods of synthesis of various heterocyclic compounds including those with pronounced biological activity are developed on the basis of enamines.

Recently,[3] a new approach to the synthesis of 1-phenyl-1,6-naphthyridines has been developed by us when studying reactions of CH acids with 4-anilino-3- and -5-formyl-pyridones (see also Ref. 4). The general character of the methods proposed and possibility of extension of their scope with the purpose of obtaining a number of new 1-aryl-1,6-naphthyridines substituted in *para*-position of the benzene ring are shown in the present study.

Earlier,[5,6] the procedure for the synthesis of various 1-alkyl- and 1-aryl-6-[2-(*N*,*N*-dimethylamino)vinyl]-4-oxo-1,4-dihydropyrimidine-5-carbonitriles **1** has been developed based on the reactions of amide acetals with the amino group of primary amides and the methyl group of 3-arylamino-2-cyanocrotonamides **2**. Pyrimidinones **1** were found[5—8] to undergo recyclization to form 4-arylamino-3-cyano-5-formylpyridin-2-ones **3** under conditions of both basic and acid hydrolysis (Scheme 1).

At present, it has been proven[8] that it is acylamidines **4** that undergo cyclization in an acid medium to form 5-formylpyridin-2-ones **5**. Nevertheless, isolation of pure acylamidines of type **4** is rather difficult since, as a rule, they are formed in a mixture with pyrimidinones **1**.

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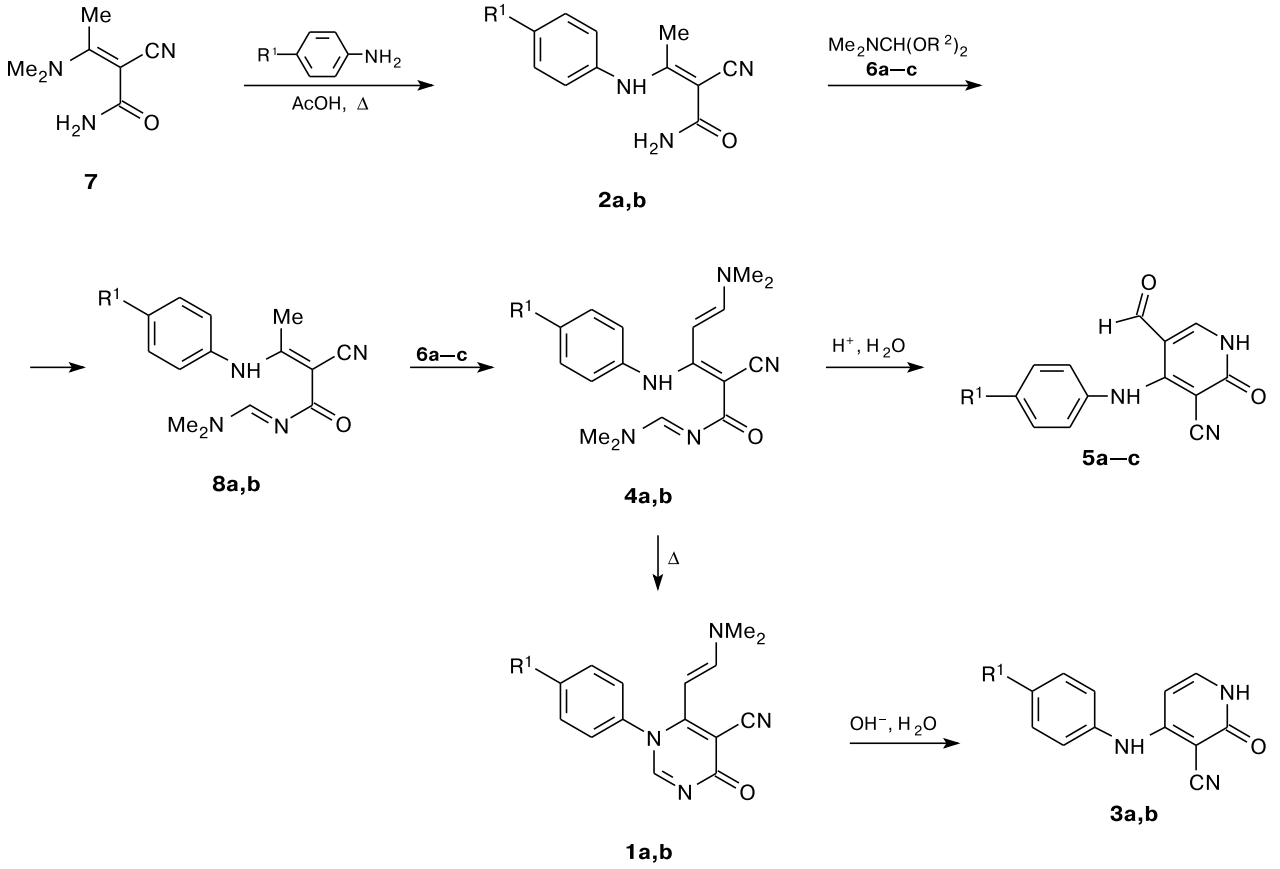
Scheme 1



R^1 = Cl (**a**), F (**b**), H (**c**); R^2 = Et (**a**), Me (**b**), Pr^i (**c**)

However, it was found[7] that individual condensation product **4a** can be isolated in high yield from the reaction of (*p*-chloroanilino)enamide **2a** with dimethylformamide diethylacetal (**6a**).

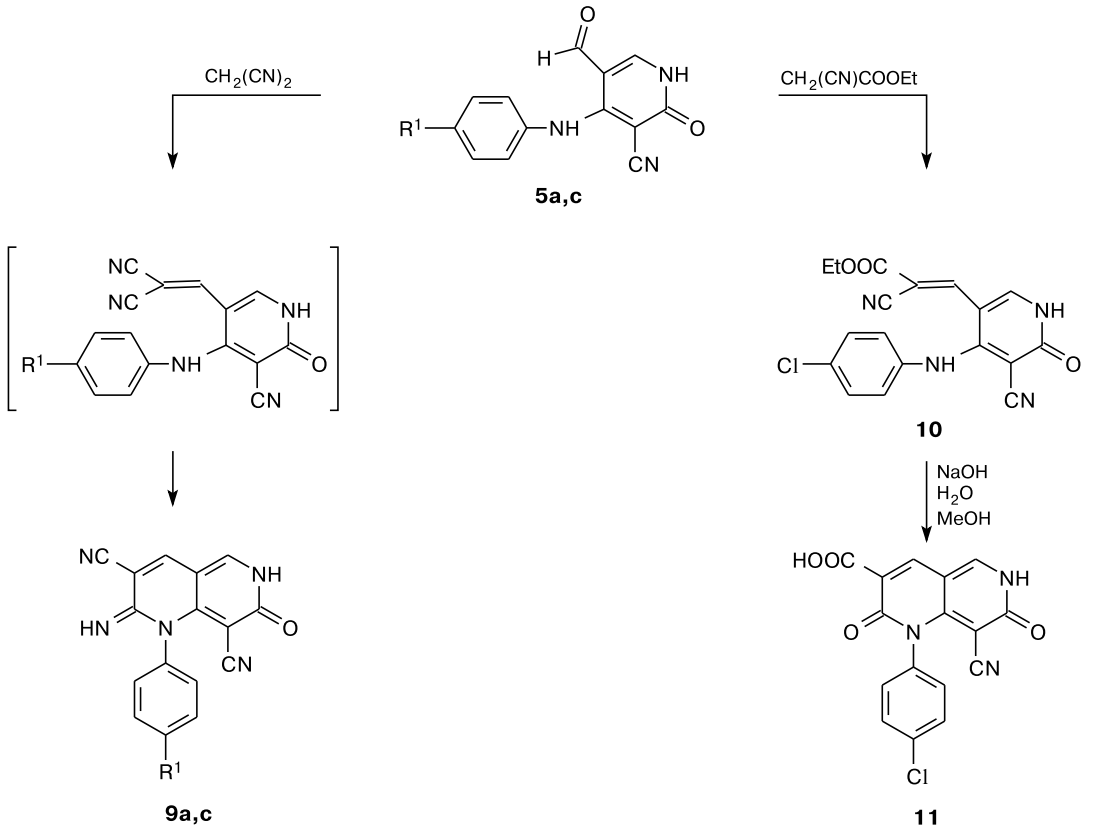
Using the known procedure,[5,9] we have synthesized enaminoamides **2a,b** by refluxing enaminoamide **7** with *p*-chloroaniline and *p*-fluoroaniline in acetic acid. Dimethylformamide dimethylacetal (**6b**) was used to prepare acylamidine **4a**. As it turned out, the crude condensation product of enaminoamide **2a** with acetal **6b** is a mixture of acylamidine **4a** and pyrimidinone **1a**, as has been noted earlier[8] for phenyl- and tolyl-substituted derivatives. To clarify the influence of the nature of the acetal (**6a** or **6b**) on the yield of acylamidine **4a**, we carried out a comparative experiment: enaminoamide **2a** was refluxed in ethanol for 40 min with dimethylformamide dimethylacetal and diethylacetal. The ratios of acylamidine **4a** and pyrimidinone **1a** in the crude products are approximately equal (^{1}H NMR): 79 : 21 for the experiment with acetal **6a** and 75 : 25 for the experiment with acetal **6b**. Sufficiently pure acylamidine **4a** could not be obtained upon recrystallization without considerable losses. Therefore, a more efficient procedure for the preparation of 5-formylpyridone **5a** involved evaporation *in vacuo* of an excess of the acetal and the solvent followed by acid hydrolysis of the reaction mixture without isolation of the individual acylamidine **4a**. 5-Formylpyridone **5a** was thus obtained in a yield of 35%.

On the contrary, the use of (*p*-fluoroanilino)enamide **2b** in the reaction with dimethylformamide dimethylacetal (**6b**) under similar conditions (short-time refluxing in EtOH) leads only to pyrimidinone **1b**, which does not allow one to synthesize 5-formylpyridone **5b**. Probably, intermediate acylamidine **4b** transforms fast into pyrimidinone **1b** on heating. In the present study, we somewhat changed the method developed earlier[8] with the purpose of preparing compound **5b**. First, the reaction of enaminoamide **2b** with acetal **6b** was carried out in dry toluene at 52 °C and amidine **8b** was obtained in high yield (65%). Thus, the primary amino group of the amide is more prone to the attack of acetal ambident cation under given conditions than the methyl group. Then amidine **8b** reacted with dimethylformamide diisopropylacetal (**6c**) under mild conditions. We failed to isolate

compound **4b** in the individual state because of its low stability under the reaction conditions and its transformation into pyrimidinone **1b**. However, 5-formylpyridone **5b** was isolated in a yield of 26% by treatment of the reaction mixture, following its concentration *in vacuo*, with 90% aqueous acetic acid. Compound **5b** can only be formed from acylamidine **4b**,[8] hence it is possible to synthesize compound **4b** using such an approach. It should be noted that it was proved necessary to use dimethylformamide diisopropylacetal (**6c**) rather then usually employed amide acetals (**6a,b**) since its higher reactivity due to better stabilization of the ambident cation[10] (the reactive species in the reactions with nucleophiles) allows reduction of the condensation temperature. This fact points to the possibility of using other, more reactive amide acetals in similar syntheses. This can lead to the systems that are inaccessible under common condensation conditions because of alternative directions of the heterocyclization.

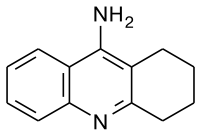
5-Formylpyridones synthesized are promising as starting compounds for the preparation of 4-arylaminopyridones derivatives containing various substituents in position 5, which are of interest from the point of view of elucidation of structure—activity relationships. At the same time, such 5-substituted pyridones can serve as precursors for various annulated heterocycles. Therefore, we carried out reactions of compound **5a** with various CH acids (Scheme 2). Thus naphthyridinone **9a** was obtained in a yield of 74% by the reaction of 5-formylpyridone **5a** with malononitrile in pyridine at 20 °C in the presence of triethylamine. Earlier,[3] it has been found that compound **9c** has the naphthyridine structure. The evidence of bicyclic structure was the presence of signals for the C atoms of two (rather then three) nitrile groups in ^{13}C NMR spectrum. In contrast to the reaction with malononitrile, the reaction of aldehyde **5a** with ethyl cyanoacetate does not result in the cyclization of the Knoevenagel reaction product: substituted vinylpyridone **10** was isolated in a yield of 72%. Earlier,[3] it has been established that compound analogous to compound **10** (a phenyl substituent at the N(1) atom) has the pyridone structure. Hydrolysis of the ethoxycarbonyl group to the carboxyl group and subsequent cyclization into naphthyridinone **11** took place upon refluxing of isolated vinylpyridone **10** in a basic medium (NaOH in aqueous methanol).

Scheme 2

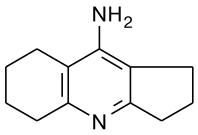


R^1 = Cl (**a**), H (**c**)

As was mentioned, recyclization of pyrimidinones under conditions of alkaline hydrolysis affords substituted 4-aminopyridones.[5–7] Compounds comprising a 4-aminopyridine or 4-aminopyridone fragment are of considerable interest due to their potential biological (including psychotropic, nootropic, *etc*.) activity.[11–13] It is sufficient to note that this class of compounds includes the well-known drugs tacrine and amiridine, which are used in the therapy of such a serious neurodegenerative disease as Alzheimer's disease.[14]



Tacrine



Amiridine

Another line of investigation of the present study was the preparation and studies of properties of other aldehydes, *viz*., 3-formylpyridones.

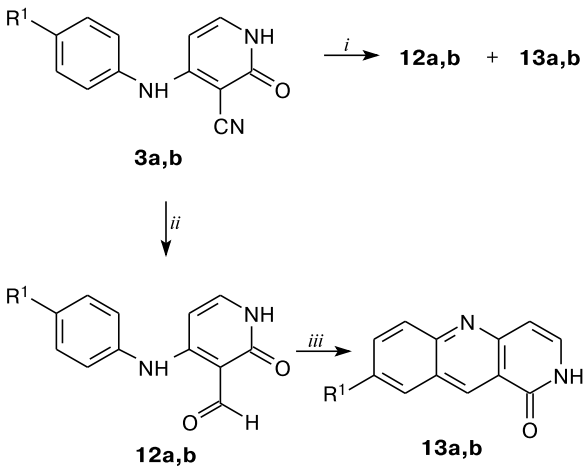
To this end, pyrimidinones **1a,b** were used, which have been obtained by refluxing enaminoamides **2a,b** with dimethylformamide dimethylacetal (**6b**) in dry toluene and in anhydrous ethanol, respectively. Pyridones **3a,b** can be prepared by both hydrolysis of the isolated pure pyrimidinones and treatment of the reaction mixture without their isolation in pure state. Compound **3a** was formed as a result of condensation of enaminoamide **2a** with dimethylformamide dimethylacetal (**6b**) followed by the treatment of reaction mixture concentrated *in vacuo* with 4% aqueous NaOH without isolation of the corresponding pyrimidinone **1a**. In contrast to **3a**, compound **3b** was obtained by alkaline hydrolysis of compound **1b**.

It is known[15] that aromatic nitriles can be transformed into aldehydes with a large excess of a Ni—Al alloy in 75% HCOOH. Refluxing of 3-cyanopyridones **3a,b** in 50% HCOOH with Ni—Al alloy (1 gram per gram of the nitrile) afforded only pure formyl derivatives **12a,b** in 43 and 45% yield, respectively (Scheme 3). The reaction of 3-cyanopyridones **3a,b** with this alloy in 85% HCOOH afforded not only 3-formylpyridones **12a,b**, but also tricyclic products **13a,b**. 3-Formylpyridones **12a,b** readily undergo cyclization to tricyclic compounds **13a,b** upon refluxing in isopropyl alcohol in the presence of piperidine.

In other words, it is possible to direct reactions to the preferred formation of either formylpyridones **12** or substituted benzonaphthyridines **13** under appropriate conditions.

Compounds **14a,b** were obtained upon reflux of 3-formylpyridones **12a,b** with malononitrile in anhydrous ethanol in the presence of triethylamine. One could suppose that the Knoevenagel reaction affords substituted vinylpyridone (**A**) or naphthyridinone (**14**) (Scheme 4).

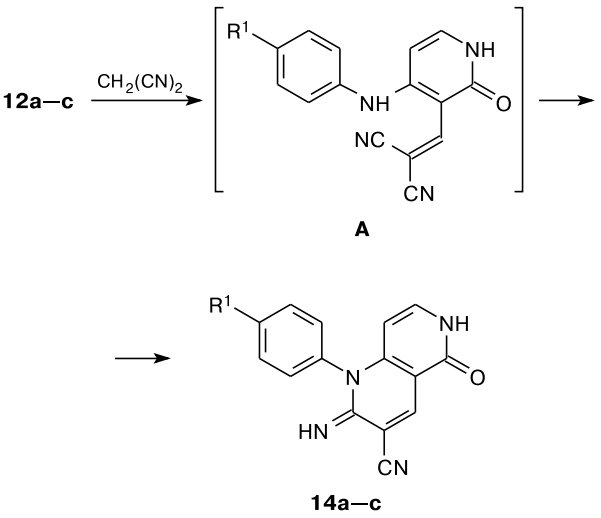
Scheme 3



R^1 = Cl (**a**), F (**b**)

Reagents and conditions: *i*. 85% HCOOH, Ni—Al alloy; *ii*. 50% HCOOH, Ni—Al alloy; *iii*. Pr^iOH + piperidine.

Scheme 4



R^1 = Cl (**a**), F (**b**), H (**c**)

Compounds **A** and **14** are isomers. The mass spectrum (ES) of compound **14a** shows peaks with *m/z* 297 $[M + H]^{+\bullet}$, 319 $[M + Na]^{+\bullet}$, 615 $[2\ M + Na]^{+\bullet}$. The mass spectrum (ES) of compound **14b** shows peaks with *m/z* 281 $[M + H]^{+\bullet}$, 303 $[M + Na]^{+\bullet}$, 561 $[2\ M + Na]^{+\bullet}$. Data from ^{1}H NMR spectroscopy do not allow determination of the exact structure of compounds **14a,b** as well. For unambiguous elucidation of their structures, X-ray diffraction analysis of compound **14a** was carried out. All geometrical characteristics of the molecule in the crystal structure of **14a** (Fig. 1) have values similar to those found in Cambridge Crystallographic Database

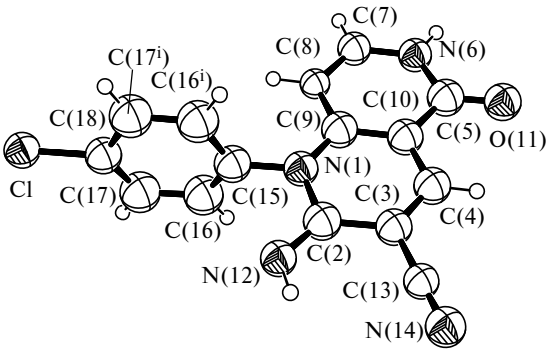


Fig. 1. Molecular structure and atom numeration of compound **14a** [code of symmetry (i) x, $1/2 - y$, z]. Spheres of atom displacements are presented with 50% probability for nonhydrogen atoms.

Table 1. Characteristics of hydrogen bonds in compound **14a**

D—H...A	*d*/Å			D—H...A angle/deg
	D—H	H...A	D...A	
N(6)—H(6)...N(12)	0.86	2.02	2.789(8)	149
N(12)—H(12)...O(11)	0.86	2.18	2.913(7)	143

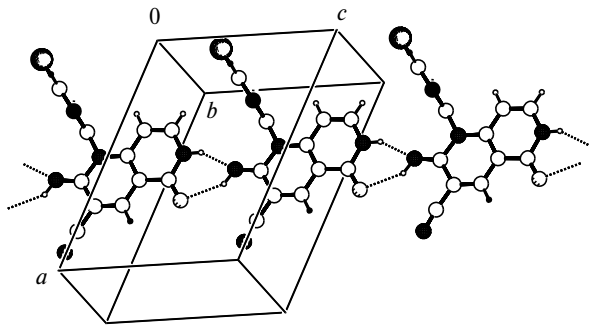
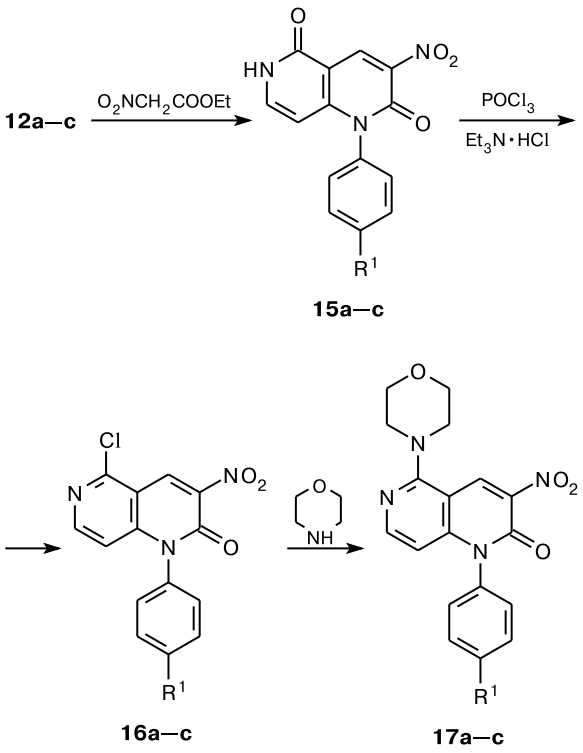


Fig. 2. Fragments of crystal packing of **14a**: molecule chains linked by hydrogen bonds (indicated by dashed lines).

(CCDC).[16] Almost all the atoms except for C(16) and C(17) with attached protons are in the mirror symmetry plane *m*. In the crystal, the amine and imine protons are involved in the intermolecular hydrogen bonds N—H...N and N—H...O (Table 1). These bonds bind the molecules in chains that are parallel to the axis *c* of the unit cell (Fig. 2). All structural data were deposited with the Cambridge Crystallographic Database (CCDC 692639)*.

1-(4-Chlorophenyl)-3-nitro-1,6-naphthyridine-2,5(1*H*,6*H*)-dione (**15a**) and 1-(4-fluorophenyl)-3-nitro-1,6-naphthyridine-2,5(1*H*,6*H*)-dione (**15b**) were prepared in 78 and 86% yields upon refluxing 3-formylpyridones **12a,b** with ethyl nitroacetate in isopropyl alcohol in the presence of a secondary amine (morpholine) (Scheme 5). 3-Nitro-1-phenyl-1,6-naphthyridine-2,5(1*H*,6*H*)-dione (**15c**) has been prepared earlier.[3]

Scheme 5



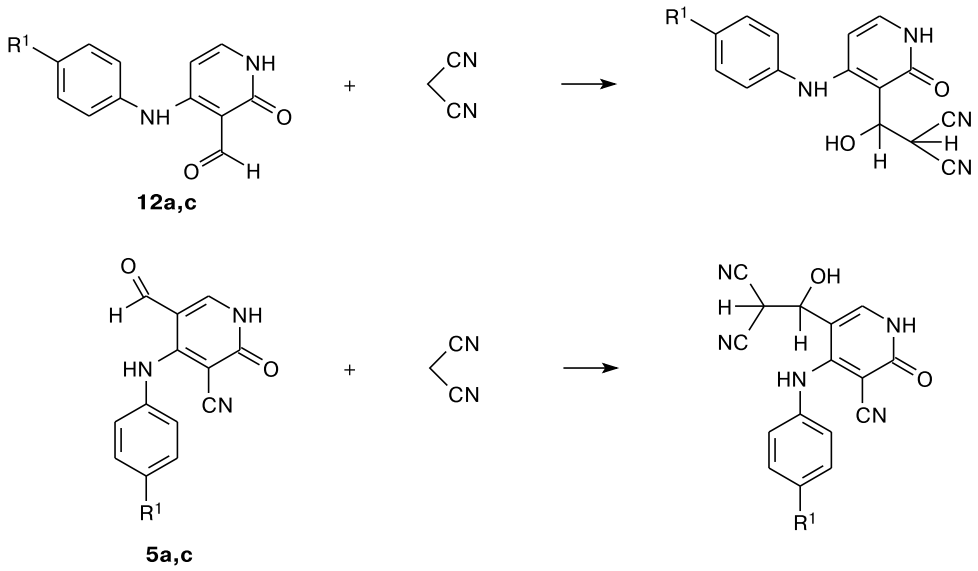
R^1 = Cl (**a**), F (**b**), H (**c**)

The corresponding 5-chloro-3-nitro-substituted naphthyridinones **16a—c** were isolated by the treatment of compounds **15a—c** with phosphoryl chloride in the presence of triethylamine hydrochloride. Triethylamine hydrochloride was used as an additional source of the chloride anions. Reactions of compounds **16a—c** with morpholine in refluxing isopropyl alcohol afforded compounds **17a—c** in high yields, this reaction was undertaken to test the ability of chlorine atom in the naphthyridine structure to undergo the nucleophilic substitution.

It was of interest to compare the reactivity of both types of the obtained pyridinecarbaldehydes with respect to nucleophilic reagents (malononitrile was chosen as the CH acid). Certainly, the presence of the electron-withdrawing nitrile group in position 3 of 5-formyl derivatives favors their enhanced reactivity. However, it should be taken into account that in this compound the cyano and formyl groups are in *meta*-position relative to each other and only inductive effects influence their interaction. One should not expect for considerable differ-

* Copies can be obtained, free of charge, on application to the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambrige CB2 1EZ, UK. Fax: +44 (0) 1223 336033. E-mail: deposit@ccdc.cam.ac.uk.

Scheme 6



ence in the rates of reactions of 3- and 5-formylpyridones with malononitrile. A comparision of the reaction rates was carried out by HPLC under competitive process conditions: DMSO, 20 °C, the ratio **5c** (or **5a**) : **12c** (or **12a**) : malononitrile was 1 : 1 : 0.25. The samples were withdrawn 2 h after beginning of the reaction. In the case of phenylderivatives (**5c** and **12c**), the ratio of the reaction products (**9c** : **14c**) was 94 : 6, and in the case of chlorophenylderivatives (**5a** and **12a**) the ratio of the reaction products (**9a** : **14a**) was 98 : 2. Therefore, in the reaction with malononitrile the reactivity of 5-formyl derivatives was considerably higher than that of 3-formyl derivatives. It can be related to the steric effects: in the case of 3-aldehyde the first step of condensation leads to a more steric hindered compound than in the case of 5-aldehyde (Scheme 6).

Thus, new 1-arylpyrimidin-4-one derivatives with a halogen substituent in the benzene ring were synthesized. Its behavior under conditions of alkaline and acid hydrolysis was studied. 4-Anilino-5-formyl-2-pyridones and 4-anilino-3-formyl-2-pyridones were obtained. A series of substituted 1,6-naphthyridines were synthesized by the Knoevenagel reaction on the basis of these 3- and 5-formylpyridones.

Experimental

The IR-spectra were recorded on an FSM-1201 instrument in Nujol mulls. The electron impact (EI) mass spectra (70 eV) were obtained on a Finnigan SSQ-710 mass spectrometer using a direct intel system, the electrospray ionization (ESI) mass spectra were recorded on a Waters ZQ-2000 mass spectrometer using a direct intel system without a chromatographic column. The ^{1}H NMR spectra were recorded on a Bruker AC-300 spectrometer in DMSO-d_6 and DMSO-d_6—CCl_4. The course of the reactions was monitored, and the purity of the compounds was checked, by TLC on Merck Silica gel 60 F_{254} plates (chloroform, chloroform—ethanol (10 : 1), ethyl acetate—ethanol (10 : 1), acetone). The melting points were determined on an Electrotermal 9100 instrument (UK). The following *N*,*N*-dimethylformamide acetals were used: dimethyl (**6b**) (purity 97%, Lancaster), diethyl (**6a**) (purity 94%, Lancaster), diisopropyl (**6c**) (purity 94%, Lancaster). Ni—Al alloy was used (Alfa Aesar, mass ratio 1 : 1).

Analysis of the reaction mixtures by HPLC was carried out on a Water Breeze system consisted of a gradient pump (Waters 1525), two-wavelength detector (Waters 2487), and a manual injector Rheodyne. Software Empower, an analytical column Phenomenex Luna C 18(2), 150×4.6 mm, and a UV detector (254 nm) were used. The eluent flow rate was 1 mL min^{-1}, temperature of the column was 20 °C, time of differentiation was 10 min. The mobile phase was methanol—buffer solution (20 : 80 for the mixture of **9c** and **14c** or 50 : 50 for the mixture **9a** and **14a**). Buffer was prepared by addition of *n*-propylamine to 0.01% aqueous formic acid to pH 5.2. Samples of the analyzed compounds and the reaction mixtures were obtained by dissolving the corresponding samples in a mixture DMSO—methanol and by dilution with the mobile phase up to 5—10 mg L^{-1} concentration, the retention time (τ/min^{-1}) was 6.8 (**9c**), 3.8 (**14c**), 2.5 (**9a**), and 4.4 (**14a**).

1-(4-Chlorophenyl)-6-[2-(dimethylamino)vinyl]-4-oxo-1,4-dihydropyrimidine-5-carbonitrile (1a). A mixture of enaminoamide **2a** (0.200 g, 0.85 mmol) and dimethylformamide dimethyl acetal (**6b**) (0.459 g, 3.85 mmol) in dry toluene (0.9 mL) was refluxed for 6 h (TLC). The reaction mixture was kept at 20 °C for 12 h, triturated, the precipitate was filtered off, washed with toluene and dried. Compound **1a** was obtained in a yield of 0.100 g (45%). M.p. 261.6—263.5 °C (Pr^iOH). IR, ν/cm^{-1}: 2178 (CN); 1628 (CO). ES MS, *m*/*z*: 301 $[M + H]^{+\bullet}$, 323 $[M + Na]^{+\bullet}$, 601 $[2\ M + H]^{+\bullet}$, 623 $[2\ M + Na]^{+\bullet}$. ^{1}H NMR (DMSO-d_6), δ: 2.61, 3.10 (both br.s, 3 H each, NMe_2); 4.02 (d, 1 H, H(6′), J_o = 12.86 Hz); 7.54, 7.63 (A_2B_2, 4 H, Ar, J_o = 8.71 Hz); 7.94 (d, 1 H, H(6″), J_o = 12.80 Hz); 8.13 (s, 1 H,

H(2)). Found (%): N, 18.60. $C_{15}H_{13}ClN_4O$. Calculated (%): N, 18.63.

6-[2-(Dimethylamino)vinyl]-1-(4-fluorophenyl)-4-oxo-1,4-dihydropyrimidine-5-carbonitrile (1b). A mixture of enaminoamide **2b** (0.100 g, 0.46 mmol) and dimethylformamide dimethyl acetal (**6b**) (0.544 g, 4.57 mmol) in absolute ethanol (2 mL) was refluxed for 2 h (TLC). The reaction mixture was cooled, the precipitate that formed was filtered off and washed with ethanol. Compound **1b** was obtained in a yield of 0.078 g (61%). M.p. 262.5—263.2 °C (Pr^iOH). IR, ν/cm^{-1}: 2205 (CN); 1643 (CO). ES MS, *m/z*: 285 $[M + H]^{+\bullet}$, 307 $[M + Na]^{+\bullet}$, 569 $[2 M + H]^{+\bullet}$, 591 $[2 M + Na]^{+\bullet}$. ^{1}H NMR (DMSO-d_6), δ: 2.59, 3.09 (both br.s, 3 H each, NMe_2); 4.01 (d, 1 H, H(6′), J_o = 12.92 Hz); 7.41 (t, 2 H, H(3′), H(3″), J_o = 8.65 Hz); 7.55—7.59 (m, 2 H, H(2′), H(2″)); 7.92 (d, 1 H, H(6″), J_o = 12.83 Hz); 8.14 (s, 1 H, H(2)). Found (%): N, 19.76. $C_{15}H_{13}FN_4O$. Calculated (%): N, 19.71.

3-(4-Chloroanilino)-2-cyanocrotonamide (2a). A mixture of 2-cyano-3-dimethylaminocrotonamide (**7**) (5.000 g, 33 mmol) and *p*-chloroaniline (4.630 g, 36 mmol) in glacial acetic acid (50 mL) was refluxed for 3 h. The reaction mixture was kept at 20 °C for 12 h. White crystals that formed were filtered off, washed with ethyl acetate, and dried. The mother liquor was concentrated *in vacuo*, the crystalline residue was washed with water, filtered off, washed with ethyl acetate, and dried. Compound **2a** was obtained in a total yield of 4.590 g (80%). M.p. 225.5—226.0 °C (EtOH) (*cf.* Ref. 7: m.p. 234 °C (EtOH)). IR, ν/cm^{-1}: 3368, 3196 (NH, NH_2); 2200 (CN); 1654 ($CONH_2$). ES MS, *m/z*: 258 $[M + Na]^{+\bullet}$, 493 $[2 M + Na]^{+\bullet}$. ^{1}H NMR (DMSO-d_6), δ: 2.22 (s, 3 H, Me); 6.80, 7.10 (both br.s, 1 H each, $CONH_2$); 7.26, 7.42 (A_2B_2, 4 H, Ar, J_o = 8.60 Hz); 12.71 (br.s, 1 H, NH).

2-Cyano-3-(4-fluoroanilino)crotonamide (2b) was prepared analogously to **2a** from compound **7** and 4-fluoroaniline. The yield was 84%. M.p. 211.5—212.4 °C (EtOH). IR, ν/cm^{-1}: 3399, 3184 (NH, NH_2); 2195 (CN); 1670 ($CONH_2$). ES MS, *m/z*: 242 $[M + Na]^{+\bullet}$, 461 $[2 M + Na]^{+\bullet}$. ^{1}H NMR (DMSO-d_6), δ: 2.17 (s, 3 H, Me); 6.80, 7.10 (both br.s, 1 H each, $CONH_2$); 7.20, 7.28 (both m, 2 H each, Ar); 12.60 (br.s, 1 H, NH). Found (%): N, 19.34. $C_{11}H_{10}FN_3O$. Calculated (%): N, 19.17.

4-(4-Chloroanilino)-2-oxo-1,2-dihydropyridine-3-carbonitrile (3a). A mixture of enaminoamide **2a** (3.000 g, 12.74 mmol) and dimethylformamide dimethyl acetal (**6b**) (4.550 g, 38.2 mmol) in absolute ethanol (26 mL) was refluxed for 4.5 h (TLC). The reaction mixture was cooled to 20 °C, the solvent was evaporated *in vacuo*, an aqueous solution of NaOH (4%, 40 mL) was added to the semicrystalline residue, and the mixture was refluxed for 1 h. The reaction mixture was cooled, diluted with 3 volumes of water, neutralized with concentrated HCl (5 mL). The precipitate that formed was filtered off, washed with water to pH 7, and dried. Compound **3a** was obtained in a yield of 1.649 g (55%). M.p. 278.3—279.1 °C (DMF—Pr^iOH, 1 : 3) (*cf.* Ref. 7: m.p. 279—281 °C (aqueous DMF)). IR, ν/cm^{-1}: 3258, 3140 (NH, NH); 2226 (CN); 1661 (CONH); 1628 (C=C). EI MS, *m/z* (I_{rel} (%)): 245 $[M]^{+\bullet}$ (100), 217 $[M - CO]^{+\bullet}$ (9), 127 $[C_6H_4ClNH_2]^{+\bullet}$ (16), 111 $[C_6H_4Cl]^{+\bullet}$ (57). ^{1}H NMR (DMSO-d_6), δ: 5.75 (d, 1 H, H(5), J_o = 7.47 Hz); 7.16, 7.30 (A_2B_2, 4 H, Ar, J_o = 8.55 Hz); 7.21 (d, 1 H, H(6), J_o = 7.53 Hz); 9.20 (br.s, 1 H, NHC(4)); 11.28 (br.s, 1 H, N(1)H).

4-(4-Fluoroanilino)-2-oxo-1,2-dihydropyridine-3-carbonitrile (3b). A mixture of enaminoamide **2b** (3.000 g, 13.7 mmol) and dimethylformamide dimethyl acetal (**6b**) (16.320 g, 136.9 mmol) in dry toluene (30 mL) was refluxed for 2.5 h (TLC). The precipitate that formed after cooling the reaction mixture to 20 °C was filtered off, washed with dry toluene and petroleum ether. Pyrimidinone **3b** was obtained in a yield of 2.753 g (71%). Aqueous solution of NaOH (4%, 27.5 mL) was added to the precipitate obtained, the mixture was refluxed for 1 h. The reaction mixture was cooled, diluted with 3 volumes of water and neutralized with concentrated HCl (20 mL). The precipitate that formed was filtered off, washed with water to pH 7, and dried. Compound **3b** was obtained in a yield of 2.109 g (95% with respect to **1b**, 67% with respect to **2b**). The mother liquor of the reaction with acetal was concentrated *in vacuo* almost to dryness. Aqueous solution of NaOH (4%, 11.5 mL) was added to the semicrystalline residue, the mixture was refluxed for 1 h, cooled, diluted with 3 volumes of water, and neutralized with concentrated HCl (5 mL). The precipitate that formed was filtered off, washed with water to pH 7, and dried. Additional crop of compound **3b** was obtained (0.666 g (21%)). Total yield was 89%. M.p. 285.9—287.2 °C (Pr^iOH). IR, ν/cm^{-1}: 3266, 3146 (NH, NH); 2224 (CN); 1665 (CONH); 1636 (C=C). ES MS, *m/z*: 230 $[M + H]^{+\bullet}$, 252 $[M + Na]^{+\bullet}$, 459 $[2 M + H]^{+\bullet}$, 481 $[2 M + Na]^{+\bullet}$. ^{1}H NMR (DMSO-d_6), δ: 5.72 (d, 1 H, H(5), J_o = 7.50 Hz); 7.13—7.27 (m, 5 H, H(6), Ar); 9.16 (br.s, 1 H, NHC(4)); 11.26 (br.s, 1 H, N(1)H). Found (%): C, 63.02; H, 3.75; N, 18.34. $C_{12}H_8FN_3O$. Calculated (%): C, 62.88; H, 3.52; N, 18.33.

3-(4-Chloroanilino)-2-cyano-5-(dimethylamino)penta-2,4-dienoic acid *N*-[(dimethylamino)methylidene]amide (4a). A mixture of enaminoamide **2a** (3.530 g, 15 mmol) and dimethylformamide dimethyl acetal (**6b**) (5.360 g, 45 mmol) in absolute ethanol (30 mL) was refluxed for 50 min. The reaction mixture was cooled, the precipitate that formed was filtered off, washed with absolute ethanol. A mixture of compound **4a** and pyrimidinone **1a** was obtained in a yield of 3.364 g. M.p. 170—172 °C. The mass spectrum of this product coincides with that of compound **1a**. ^{1}H NMR (DMSO-d_6), δ: 2.89 (br.s, 6 H, NMe_2); 3.06, 3.15 (both br.s, 3 H each, NMe_2); 4.74 (d, 1 H, H(4), J_o = 13.12 Hz); 7.21, 7.32 (A_2B_2, 4 H, Ar, J_o = 8.50 Hz); 7.41 (d, 1 H, H(5), J_o = 13.10 Hz); 8.37 (s, 1 H, NC<u>H</u>NMe_2); 12.44 (br.s, 1 H, NH).

4-(4-Chloroanilino)-5-formyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (5a). A mixture of enaminoamide **2a** (0.606 g, 4 mmol) and dimethylformamide dimethyl acetal (**6b**) (5.380 g, 41 mmol) was refluxed for 15 min at 76 °C. The reactin mixture was cooled to 20 °C, and concentrated *in vacuo*. Glacial acetic acid (6 mL) and water (0.6 mL) were added to the dry residue. The yellow solution that formed was kept at 20 °C for 3 days. The precipitate that formed was filtered off and washed with ethyl acetate. Compound **5a** was obtained in a yield of 0.368 g (35%). M.p. 285.9—287.2 °C (DMF) (*cf.* Ref. 17: m.p. 290 °C (decomp., Pr^iOH—DMF, 3 : 2)). IR, ν/cm^{-1}: 3198, 3090 (NH); 2218 (CN); 1692 (COH); 1645 (CONH). ES MS, *m/z*: 296 $[M + Na]^{+\bullet}$, 569 $[2 M + Na]^{+\bullet}$, 244 $[M - CHO]^{+\bullet}$.

4-(4-Fluoroanilino)-5-formyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (5b). Dimethylformamide diisopropyl acetal (**6c**) (1.68 mL, 0.765 mmol) was added to a suspension of acylamidine **8b** (0.700 g, 0.255 mmol) in dry toluene (5 mL). The mixture obtained was stirred for 2 h at 52—54 °C. The precipitate that formed was filtered off, the starting acylamidine **8b** was recovered in a yield of 0.340 g. The mother liquor was concentrated *in vacuo* almost to dryness. Aqueous acetic acid (90%, 1 mL)

was added to the oily residue. The yellow solution that formed was kept at 20 °C for 2 days. White precipitate that formed was filtered off. Compound **5b** was obtained in a yield of 0.170 g (26% relative to the original amount of compound **8b**). M.p. 322.5 °C (decomp., Pr^iOH—DMF (3 : 2)). ES MS, *m/z*: 258 $[M + H]^{+\bullet}$, 280 $[M + Na]^{+\bullet}$, 537 $[2 M + Na]^{+\bullet}$. ^1H NMR (DMSO-d_6), δ: 7.20, 7.38 (both m, 2 H each, Ar); 8.39 (s, 1 H, C(6)); 9.59 (s, 1 H, COH); 10.51 (br.s, 1 H, N(1)H); 12.32 (br.s, 1 H, NHC(4)). Found (%): C, 60.63; H, 3.13; N, 16.33. $C_{13}H_8FN_3O_2$. Calculated (%): C, 60.70; H, 3.14; N, 16.34.

***N*-Dimethylaminomethylidene-3-(4-chloroanilino)-2-cyanocrotonamide (8a).** Dimethylformamide dimethyl acetal (**6b**) (1.67 mL, 12.484 mmol) was added to a suspension of enaminoamide **2a** (0.490 g, 2.081 mmol) in absolute ethanol (7 mL). The solution obtained was stirred for 3.5 h at 54 °C. The precipitate that formed after cooling of the reaction mixture was filtered off and washed with absolute ethanol. Compound **8a** was obtained in a yield of 0.453 g (75%). M.p. 128.5—129.2 °C (EtOH). IR, ν/cm^{-1}: 3400 (NH), 2205 (CN), 1630 (CO). ES MS, *m/z*: 291 $[M + H]^{+\bullet}$, 581 $[2 M + H]^{+\bullet}$. ^1H NMR (DMSO-d_6), δ: 2.27 (s, 3 H, C(4)H_3); 3.08, 3.20 (both s, 3 H each, NMe_2); 7.27, 7.42 (A_2B_2, 4 H, Ar, J_o = 8.61 Hz); 8.45 (s, 1 H, NC<u>H</u>NMe_2); 12.99 (br.s, 1 H, NH). Found (%): C, 57.85; H, 5.46; N, 19.14. $C_{14}H_{15}ClN_4O$. Calculated (%): C, 57.83; H, 5.20; N, 19.27.

***N*-Dimethylaminomethylidene-3-(4-fluoroanilino)-2-cyanocrotonamide (8b).** Dimethylformamide dimethyl acetal (**6b**) (7.32 mL, 54.792 mmol) was added to a suspension of enaminoamide **2b** (2.000 g, 9.132 mmol) in dry toluene (25 mL). The solution obtained was stirred for 1.5 h at 52 °C. White precipitate that formed was filtered off and washed with dry toluene. Compound **8b** was obtained in a yield of 1.616 g (65%). M.p. 141.3—142.1 °C (EtOH). IR, ν/cm^{-1}: 3400 (NH), 2199 (CN), 1626 (C=C). ES MS, *m/z*: 275 $[M + H]^{+\bullet}$, 297 $[M + Na]^{+\bullet}$, 549 $[2 M + H]^{+\bullet}$. ^1H NMR (DMSO-d_6), δ: 2.21 (s, 3 H, C(4)H_3); 3.02, 3.16 (both s, 3 H each, NMe_2); 7.25, 7.34 (both m, 2 H each, Ar); 8.47 (s, 1 H, NC<u>H</u>NMe_2); 12.88 (br.s, 1 H, NH). Found (%): C, 61.38; H, 5.56; N, 20.48. $C_{14}H_{15}FN_4O$. Calculated (%): C, 61.30; H, 5.51; N, 20.43.

1-(4-Chlorophenyl)-3,8-dicyano-2-imino-1,6-naphthyridin-7(1*H*,6*H*)-one (9a). Malononitrile (0.013 g, 0.2 mmol) and triethylamine (0.02 mL, 0.2 mmol) were added to a suspension of 5-formylpyridone **5a** (0.038 g, 0.139 mmol) in pyridine (0.38 mL). The reaction mixture was kept for 3 days at 20 °C (TLC). The precipitate that formed was filtered off and washed with propan-2-ol. Compound **9a** was obtained in a yield of 0.033 g (74%). M.p. 287.1—287.5 °C (Pr^iOH—DMF (5 : 1)). IR, ν/cm^{-1}: 3312, 3289 (NH); 2228, 2210 (CN); 1663 (CONH), 1616 (C=C). ES MS, *m/z*: 322 $[M + H]^{+\bullet}$, 344 $[M + Na]^{+\bullet}$, 665 $[2 M + Na]^{+\bullet}$. ^1H NMR (DMSO-d_6), δ: 7.45, 7.62 (A_2B_2, 4 H, Ar, J_o = 8.34 Hz); 8.17 (s, 1 H, H(4)); 8.29 (s, 1 H, H(5)). Found (%): C, 59.77; H, 2.90; N, 21.82. $C_{16}H_8ClN_5O$. Calculated (%): C, 59.73; H, 2.51; N, 21.77.

4-(4-Chloroanilino)-5-(2-cyano-2-ethoxycarbonylvinyl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (10). A mixture of 5-formylpyridone **5a** (0.500 g, 1.83 mmol), ethyl cyanoacetate (0.207 g, 1.83 mmol), and triethylamine (0.18 mL) in pyridine (5 mL) was kept for 48 h at 20 °C (TLC). The precipitate that formed was filtered off, washed with propan-2-ol, and benzene. Compound **10** was obtained in a yield of 0.345 g (72%). M.p. 296.7—297.1 °C (DMF). IR, ν/cm^{-1}: 3306, 3164 (NH); 2214 (CN); 1697 (CONH). ES MS, *m/z*: 369 $[M + H]^{+\bullet}$, 391 $[M + Na]^{+\bullet}$, 759 $[2 M + Na]^{+\bullet}$. ^1H NMR (DMSO-d_6), δ: 1.39 (t, 3 H, $COOCH_2C\underline{H}_3$, J_o = 7.10 Hz); 4.35 (q, 2 H, $COOC\underline{H}_2CH_3$, J_o = 7.10 Hz); 7.59, 7.69 (A_2B_2, 4 H, Ar, J_o = 8.44 Hz); 8.65, 8.73 (both br.s, 1 H each, H(5′), H(6)); 9.50 (br.s, 1 H, NH(1)). Found (%): N, 15.14. $C_{18}H_{13}ClN_4O_3$. Calculated (%): N, 15.19.

1-(4-Chlorophenyl)-8-cyano-2,7-dioxo-1,2,6,7-tetrahydro-1,6-naphthyridine-3-carboxylic acid (11). Compound **10** (0.150 g, 0.407 mmol) was added to 10 mL of solution of NaOH (2 g) in methanol (20 mL) and water (10 mL). The mixture obtained was refluxed for 10.5 h. The reaction mixture was cooled to 20 °C. The solution of sodium salt obtained was acidified with concentrated HCl to pH 1 and kept for 0.5 h. The precipitate that formed was filtered off, and washed with water. Compound **11** was obtained in a yield of 0.110 g (80%). M.p. 369.6—371.2 °C (Pr^iOH—DMF, 6 : 1). IR, ν/cm^{-1}: 3490 (OH); 3270 (NH); 2216 (CN); 1742 (COOH); 1682 (CO). ES MS, *m/z*: 342 $[M + H]^{+\bullet}$, 364 $[M + Na]^{+\bullet}$, 705 $[2 M + Na]^{+\bullet}$. ^1H NMR (DMSO-d_6), δ: 7.45, 7.57 (A_2B_2, 4 H, Ar, J_o = 8.83 Hz); 8.71, 8.77 (both s, 1 H each, H(4), H(5)). Found (%): N, 12.03. $C_{16}H_8ClN_3O_4$. Calculated (%): N, 12.30.

4-(4-Chloroanilino)-2-oxo-1,2-dihydropyridine-3-carbaldehyde (12a). An Ni—Al alloy (1 g) was added to a suspension of pyridone **3a** (1 g, 4.073 mmol) in 50 % HCOOH (35 mL). The reaction mixture was refluxed with stirring for 6 h (TLC). The precipitate was filtered off after cooling the reaction mixture to 20 °C, washed with small amount of 50% HCOOH and water. The crude precipitate that represented a mixture of inorganic salts and the reaction product was extracted with DMF (4×20 mL), the solids were filtered off, the filtrate was concentrated *in vacuo* to dryness, the residue (crystalline precipitate) was triturated with petroleum ether, filtered off, and washed with petroleum ether. Compound **12a** was obtained in a yield of 0.433 g (43%). M.p. 301—303 °C (DMF). (We succeeded in isolation of only small amounts of the starting pyridone from the mother liquor of the reaction mixture.) IR, ν/cm^{-1}: 3146, 3057 (NH); 1651 (COH); 1620 (CONH). ES MS, *m/z*: 249 $[M + H]^{+\bullet}$, 271 $[M + Na]^{+\bullet}$, 519 $[2 M + Na]^{+\bullet}$, 767 $[3 M + Na]^{+\bullet}$. ^1H NMR (DMSO-d_6), δ: 5.87 (d, 1 H, H(5), J_o = 7.53 Hz); 7.32, 7.47 (A_2B_2, 4 H, Ar, J_o = 8.70 Hz); 7.38 (d, 1 H, H(6), J_o = 7.50 Hz); 10.03 (s, 1 H, COH); 11.17 (br.s, 1 H, NH(1)); 11.63 (br.s, 1 H, NHC(4)). Found (%): C, 57.94; H, 3.77; N, 11.38. $C_{12}H_9ClN_2O_2$. Calculated (%): C, 57.96; H, 3.65; N, 11.27.

4-(4-Fluoroanilino)-2-oxo-1,2-dihydropyridine-3-carbaldehyde (12b) was prepared analogously to **12a** from compound **3b**. The reaction time was 26 h. The yield was 45%. M.p. 386.5 °C (EtOH). IR, ν/cm^{-1}: 3140, 3065 (NH); 1647 (COH); 1624 (CONH). ES MS, *m/z*: 233 $[M + H]^{+\bullet}$, 255 $[M + Na]^{+\bullet}$, 487 $[2 M + Na]^{+\bullet}$, 719 $[3 M + Na]^{+\bullet}$. ^1H NMR (DMSO-d_6), δ: 5.78 (d, 1 H, H(5), J_o = 7.53 Hz); 7.18—7.33 (m, 5 H, H(6), Ar); 10.02 (s, 1 H, COH); 11.08 (br.s, 1 H, NH(1)); 11.62 (br.s, 1 H, NHC(4)). Found (%): C, 62.14; H, 4.48; N, 12.37. $C_{12}H_9FN_2O_2$. Calculated (%): C, 62.07; H, 3.91; N, 12.06.

8-Chloro-1,2-dihydrobenzo[*b*]-1,6-naphthyridine-1-one (13a). Piperidine (0.26 mL, 3.06 mmol) was added to a solution of 3-formylpyridone **12a** (0.150 g, 0.602 mmol) in propan-2-ol (6 mL). The reaction mixture was refluxed for 25 h (TLC). The precipitate that formed after cooling the reaction mixture to 20 °C was filtered off and washed with Pr^iOH. Compound **13a**

was obtained in a yield of 0.130 g (94%). M.p. 357.5 °C (DMF). IR, ν/cm^{-1}: 3165 (NH); 1665 (CONH). ES MS, *m/z*: 231 $[M + H]^{+\bullet}$, 253 $[M + Na]^{+\bullet}$, 483 $[2 M + Na]^{+\bullet}$. ^{1}H NMR (DMSO-d_6), δ: 6.63 (d, 1 H, H(4), J_o = 7.5 Hz); 7.41, 7.81, 8.03 (all m, 1 H each, H(3), H(7), H(6)); 8.26 (s, 1 H, H(9)); 9.18 (s, 1 H, H(10)); 11.32 (br.s, 1 H, N(2)H). Found (%): C, 62.49; H, 3.37; N, 12.12. $C_{12}H_7ClN_2O$. Calculated (%): C, 62.49; H, 3.06; N, 12.15.

8-Fluoro-1,2-dihydrobenzo[*b*]-1,6-naphthyridine-1-one (13b). *Method A*. An Ni—Al alloy (0.2 g) was added to a suspension of pyridone **7b** (0.2 g, 0.873 mmol) in 80% HCOOH (19 mL), the reaction mixture was refluxed with stirring for 35 h. Solids were filtered off after cooling the reaction mixture to 20 °C, washed with small amount of 85% HCOOH. The mother liquor was concentrated *in vacuo* to dryness. Water (3 mL) was added to the crystalline residue and the mixture was kept at 20 °C for 2 days. The precipitate that formed (a mixture of compounds **12b** and **13b**, TLC), was filtered off. The yield of this mixture was 0.070 g. The filtrate was concentrated *in vacuo* to dryness, the residue was triturated with acetone. The precipitate was filtered off, washed with acetone. The yield of compound **13b** was 0.040 g (22.4%). ES MS, *m/z*: 215 $[M + H]^{+\bullet}$, 237 $[M + Na]^{+\bullet}$, 253 $[M + K]^{+\bullet}$.

Method B is analogous to the method of preparation of compound **13a**. The reaction time was 40 h. The yield was 91%. M.p. 270.2—270.6 °C (EtOH). IR, ν/cm^{-1}: 3169 (NH); 1665 (CONH). ^{1}H NMR (DMSO-d_6), δ: 6.63 (d, 1 H, H(4), J_o = 7.50 Hz); 7.37, 7.72, 7.91, 8.08 (all m, 1 H each, H(6), H(3), H(9), H(7)); 9.19 (s, 1 H, H(10)); 11.28 (br.s, 1 H, N(2)H). Found (%): C, 67.15; H, 3.62; N, 13.05. $C_{12}H_7FN_2O$. Calculated (%): C, 67.29; H, 3.29; N, 13.08.

1-(4-Chlorophenyl)-3-cyano-2-imino-1,6-naphthyridin-5(2*H*,6*H*)-one (14a). Malononitrile (0.067 g, 1.007 mmol) and triethylamine (0.05 mL) were added to a suspension of 3-formylpyridone **12a** (0.100 g, 0.402 mmol) in absolute ethanol (3 mL). The reaction mixture was refluxed for 12 h (TLC). The precipitate that formed was filtered off and washed with ethanol. Compound **14a** was obtained in a yield of 0.084 g (71%). M.p. 300 °C (DMF). IR, ν/cm^{-1}: 3279, 3123 (NH); 2224 (CN); 1672 (CONH); 1634 (C=C). ES MS, *m/z*: 297 $[M + H]^{+\bullet}$, 319 $[M + Na]^{+\bullet}$, 615 $[2 M + Na]^{+}$. ^{1}H NMR (DMSO-d_6), δ: 5.20 (d, 1 H, H(8), J_o = 7.44 Hz); 6.39, 7.17 (both br.s, 1 H, NH=C(2)); 7.36 (d, 1 H, H(7), J_o = 7.44 Hz); 7.45, 7.72 (A_2B_2, 4 H, Ar, J_o = 8.58 Hz); 8.16 (s, 1 H, H(4)); 11.78 (br.s, 1 H, NH(6)). Found (%): C, 60.74; H, 3.08; N, 18.79. $C_{15}H_9ClN_4O$. Calculated (%): C, 60.72; H, 3.06; N, 18.88.

The structure of compound **14a** was established by powder X-ray diffraction.[18] Powder diagram was measured in the Guinier camera "Huber G670" containing bent germanium monochromator. The positions of first 22 peaks were refined on the powder diagram. Using these positions, indicating in the monoclinic cell was carried out with the TREOR90 program.[19] Systematical reductions revealed by refinement of the powder diagram using the Pauli method[20] by the MRIA[21] program were consistent with two space groups: $P2_1$ and $P2_1/m$. The crystal structure of compound **14a** was solved by the method of systematic search[22] in the $P2_1$ group. Rigid three-dimensional molecule model obtained as a result of the optimization by the density functional method using the PRIRODA[23] program was used. Then the solution obtained was refined by the Rietveld method using the MRIA program, peak profiles were described by the modified Voight function[24] taking into account anisotropy of the peak broadening.[25] Texture effects caused by prior alignment of crystals were considered within the limits of the March—Dollas model[26] (the direction of the prior alignment was 010, refined value of parameter *r* was 1.022(8)) In the refinement, restriction to the permissible deflections of the interatomic distances in the molecule and to the planarity of the rings were applied. Parameters of thermal fluctuations of nonhydrogen atoms were refined in an isotropic approximation. After the first cycle of refinement, the crystal structure was transformed into centrosymmetrical three-dimensional $P2_1/m$ group using the PLATON[27] program; after that refinement was continued. Hydrogen atoms were placed at the calculated positions and were not refined. The principal crystallographic characteristics and experimental parameters of compound **14a** are given in Table 2. The experimental powder diagram and the difference curve as a result of refinement using the Rietveld method are shown in Fig. 3.

3-Cyano-1-(4-fluorophenyl)-2-imino-1,6-naphthyridin-5(2*H*,6*H*)-one (14b) was prepared analogously to **14a** from compound **12b**. The yield was 97%. M.p. 302 °C (DMF). IR, ν/cm^{-1}: 3281, 3070 (NH); 2222 (CN); 1672 (CO); 1634 (CONH). ES MS, *m/z*: 281 $[M + H]^{+\bullet}$, 303 $[M + Na]^{+\bullet}$, 561 $[2 M + Na]^{+}$. ^{1}H NMR (DMSO-d_6), δ: 5.19 (d, 1 H, H(8), J_o = 6.87 Hz); 6.32, 7.17 (both br.s, 1 H, NH=C(2)); 7.37 (d, 1 H, H(7), J_o = 7.50 Hz); 7.48 (m, 4 H, Ar); 8.14 (s, 1 H, H(4)); 11.68 (br.s, 1 H, NH(6)). Found (%): C, 64.19; H, 3.38; N, 19.97. $C_{15}H_9FN_4O$. Calculated (%): C, 64.29; H, 3.24; N, 19.99.

Table 2. Crystallographic characteristics of compound **14a**

Parameter	Value
Molecular formula	$C_{15}H_9ClN_4O$
Crystal system	Monoclinic
Space group	$P2_1/m$
a/Å	11.9604(11)
b/Å	6.7697(5)
c/Å	8.8512(8)
α/deg	90
β/deg	109.765(12)
γ/deg	90
V/Å^3	674.45(10)
M_{20}*	29
F_{30}*	55 (0.010, 37)
Z	2
d_{calc}/g cm^{-3}	1.461
Radiation	Cu-Kα$_1$
Wavelength/Å	1.5406
$2\theta_{min}$—$2\theta_{max}$/deg	4.00—100.50
Step of measurement/deg	0.01
R_p*	0.0237
R_{wp}*	0.0325
R_{exp}*	0.0100
χ^{2}*	9.345

* Indicators of indication quality M_{20} (see Ref. 28) and F_{30} (see Ref. 29) were determined previously, R_p, R_{wp}, R_{exp} and χ^2 — see Ref. 30.

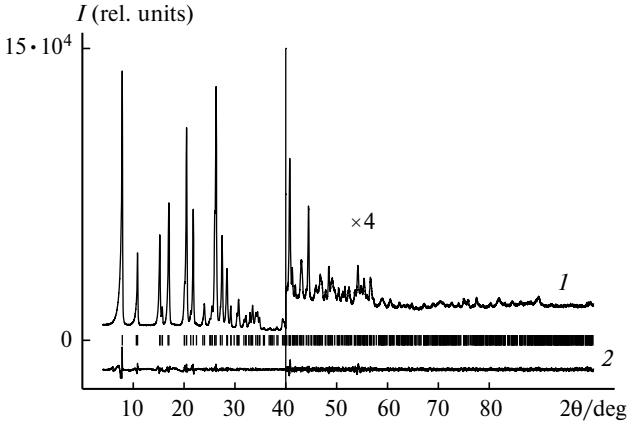


Fig. 3. The result of elucidation of crystal structure of compound **14a** by the Rietveld method: experimental curve (*1*), the difference between the experimental and calculated curves as a result of refinement (*2*); high-angle area ($2\theta > 40°$) is presented on a large scale. The calculated positions of reflexes are indicated as vertical segments.

1-(4-Chlorophenyl)-3-nitro-1,6-naphthyridine-2,5(1*H*,6*H*)-dione (15a). A mixture of 3-formylpyridone **12a** (0.100 g, 0.402 mmol), ethyl nitroacetate (0.107 g, 0.803 mmol), and morpholine (0.086 g, 0.987 mmol) in Pr^iOH (7 mL) was refluxed for 6 h (TLC). The reaction mixture was cooled to 20 °C. The precipitate was filtered off, and washed with Pr^iOH. Compound **15a** was obtained in a yield of 0.100 g (78%). M.p. 325 °C (Pr^iOH). IR, ν/cm^{-1}: 3194 (NH); 1697, 1672 (CONH); 1618 (C=C); 1518 (NO_2). ES MS, *m/z*: 318 $[M + H]^{+\bullet}$, 340 $[M + Na]^{+\bullet}$, 657 $[2 M + Na]^+$. ^1H NMR (DMSO-d_6), δ: 5.43 (d, 1 H, H(8), J_o = 7.47 Hz); 7.41, 7.67 (A_2B_2, 4 H, Ar, J_o = 8.28 Hz); 7.51 (d, 1 H, H(7), J_o = 7.29 Hz); 8.89 (s, 1 H, H(4)); 12.07 (br.s, 1 H, NH(6)). Found (%): C, 52.90; H, 2.70; N, 13.29. $C_{14}H_8ClN_3O_4$. Calculated (%): C, 52.93; H, 2.54; N, 13.23.

1-(4-Fluorophenyl)-3-nitro-1,6-naphthyridine-2,5(1*H*,6*H*)-dione (15b) was prepared analogously to **15a** from compound **12b**. The yield was 86%. M.p. 350.3 °C (Pr^iOH). IR, ν/cm^{-1}: 3237 (NH); 1699, 1672 (CONH); 1618 (C=C); 1512 (NO_2). ES MS, *m/z*: 302 $[M + H]^{+\bullet}$, 324 $[M + Na]^{+\bullet}$, 625 $[2 M + Na]^+$. ^1H NMR (DMSO-d_6), δ: 5.41 (d, 1 H, H(8), J_o = 7.49 Hz); 7.42 (m, 4 H, Ar); 7.51 (d, 1 H, H(7), J_o = 7.51 Hz); 8.89 (s, 1 H, H(4)); 12.07 (br.s, 1 H, NH(6)). Found (%): C, 55.63; H, 2.78; N, 13.87. $C_{14}H_8FN_3O_4$. Calculated (%): C, 55.82; H, 2.68; N, 13.95.

5-Chloro-1-(4-chlorophenyl)-3-nitro-1,6-naphthyridin-2(1*H*)-one (16a). A mixture of compound **15a** (0.100 g, 0.315 mmol), triethylamine hydrochloride (0.043 g, 0.313 mmol), and phosphoryl chloride (1.2 mL) was refluxed for 4 h (TLC). The reaction mixture was cooled to 20 °C, and concentrated *in vacuo* to dryness. The residue was triturated with toluene and concentrated *in vacuo* to dryness. The residue was triturated with small amount of propan-2-ol and kept at 20 °C for 24 h. The precipitate was filtered off, compound **16a** was obtained in a yield of 0.075 g (71%). M.p. 290—292 °C (Pr^iOH). IR, ν/cm^{-1}: 1703 (CON); 1622 (C=C); 1530 (NO_2). ES MS, *m/z*: 336 $[M + H]^{+\bullet}$, 358 $[M + Na]^{+\bullet}$, 693 $[2 M + Na]^+$. ^1H NMR (DMSO-d_6), δ: 6.59 (d, 1 H, H(8), J_o = 5.98 Hz); 7.46, 7.70 (A_2B_2, 4 H, Ar, J_o = 8.53 Hz); 8.31 (d, 1 H, H(7), J_o = 6.01 Hz); 8.97 (s, 1 H, H(4)). Found (%): C, 49.91; H, 2.11; N, 12.56. $C_{14}H_7Cl_2N_3O_3$. Calculated (%): C, 50.03; H, 2.10; N, 12.50.

5-Chloro-1-(4-fluorophenyl)-3-nitro-1,6-naphthyridin-2(1*H*)-one (16b) was prepared analogously to **16a** from compound **15b**. The yield was 88%. M.p. 230 °C (Pr^iOH). IR, ν/cm^{-1}: 1697, 1688 (CO); 1616 (C=C); 1532 (NO_2). ES MS, *m/z*: 320 $[M + H]^{+\bullet}$, 342 $[M + Na]^{+\bullet}$, 661 $[2 M + Na]^+$. ^1H NMR (DMSO-d_6), δ: 6.57 (d, 1 H, H(8), J_o = 6.10 Hz); 7.44 (m, 4 H, Ar); 8.30 (d, 1 H, H(7), J_o = 5.98 Hz); 8.95 (s, 1 H, H(4)). Found (%): C, 52.60; H, 2.22; N, 13.19. $C_{14}H_7FClN_3O_3$. Calculated (%): C, 52.60; H, 2.21; N, 13.14.

5-Chloro-3-nitro-1-phenyl-1,6-naphthyridin-2(1*H*)-one (16c) was prepared analogously to **16a** from compound **15c** (see Ref. 3). The yield was 70%. M.p. 180—181.5 °C (Pr^iOH). ES MS, *m/z*: 302 $[M + H]^{+\bullet}$, 324 $[M + Na]^{+\bullet}$, 625 $[2 M + Na]^+$, 255 $[M - NO_2]^+$. ^1H NMR (DMSO-d_6), δ: 6.52 (d, 1 H, H(8), J_o = 6.03 Hz); 7.46, 7.66 (both m, 2 H each, 3 H, Ph); 8.34 (d, 1 H, H(7), J_o = 6.02 Hz); 9.05 (s, 1 H, H(4)). Found (%): N, 14.13. $C_{14}H_8ClN_3O_3$. Calculated (%): N, 13.93.

1-(4-Chlorophenyl)-5-morpholino-3-nitro-1,6-naphthyridin-2(1*H*)-one (17a). Morpholine (0.104 g, 1.19 mmol) was added to a suspension of compound **16a** (0.100 g, 0.299 mmol) in Pr^iOH (2 mL). The reaction mixture was refluxed for 1.5 h (TLC). The precipitate that formed after cooling the reaction mixture to 20 °C was filtered off and washed with Pr^iOH. Compound **17a** was obtained in a yield of 0.104 g (91%). M.p. 231.0—231.8 °C (Pr^iOH—DMF, 10 : 1). IR, ν/cm^{-1}: 1692 (CO); 1518 (NO_2). ES MS, *m/z*: 387 $[M + H]^{+\bullet}$, 409 $[M + Na]^{+\bullet}$, 795 $[2 M + Na]^+$. ^1H NMR (DMSO-d_6), δ: 3.47 (t, 4 H, $N(CH_2)_2$, J_o = 4.02 Hz); 3.82 (t, 4 H, $O(CH_2)_2$, J_o = 4.13 Hz); 6.07 (d, 1 H, H(8), J_o = 5.90 Hz); 7.40, 7.67 (A_2B_2, 4 H, Ar, J_o = 8.43 Hz); 8.12 (d, 1 H, H(7), J_o = 5.98 Hz); 8.78 (s, 1 H, H(4)). Found (%): C, 56.04; H, 4.05; N, 14.41. $C_{18}H_{15}ClN_4O_4$. Calculated (%): C, 55.90; H, 3.91; N, 14.49.

1-(4-Fluorophenyl)-5-morpholino-3-nitro-1,6-naphthyridin-2(1*H*)-one (17b) was prepared analogously to **17a** from compound **16b**. The yield was 89%. M.p. 217.7—218 °C (Pr^iOH). IR, ν/cm^{-1}: 1680 (CO); 1535 (NO_2). ES MS, *m/z*: 371 $[M + H]^{+\bullet}$, 393 $[M + Na]^{+\bullet}$, 763 $[2 M + Na]^+$. ^1H NMR (DMSO-d_6), δ: 3.46 (t, 4 H, $N(CH_2)_2$, J_o = 4.52 Hz); 3.83 (t, 4 H, $O(CH_2)_2$, J_o = 4.23 Hz); 6.06 (d, 1 H, H(8), J_o = 6.00 Hz); 7.42 (m, 4 H, Ar); 8.13 (d, 1 H, H(7), J_o = 5.90 Hz); 8.79 (s, 1 H, H(4)). Found (%): C, 58.00; H, 4.12; N, 14.73. $C_{18}H_{15}FN_4O_4$. Calculated (%): C, 58.38; H, 4.08; N, 15.13.

5-Morpholino-3-nitro-1-phenyl-1,2-dihydro-1,6-naphthyridin-2(1*H*)-one (17c) was prepared analogously to **17a** from compound **16c**. The yield was 32%. M.p. 227—228 °C (Pr^iOH). IR, ν/cm^{-1}: 1688 (CO); 1518 (NO_2). ES MS, *m/z*: 353 $[M + H]^{+\bullet}$, 375 $[M + Na]^{+\bullet}$, 705 $[2 M + H]^+$, 727 $[2 M + Na]^+$. ^1H NMR (DMSO-d_6), δ: 3.46 (t, 4 H, $N(CH_2)_2$, J_o = 4.02 Hz); 3.83 (t, 4 H, $O(CH_2)_2$, J_o = 4.91 Hz); 6.03 (d, 1 H, H(8), J_o = 5.91 Hz); 7.33, 7.63 (both m, 2 H each, 3 H, Ph); 8.10 (d, 1 H, H(7), J_o = 5.86 Hz); 8.78 (s, 1 H, H(4)). Found (%): C, 60.92; H, 4.60; N, 15.39. $C_{18}H_{16}N_4O_4$. Calculated (%): C, 61.36; H, 4.58; N, 15.90.

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