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Heterocyclization of Michael Adducts of β-Diketones with Arylmethylidene Derivatives of Malononitrile Dimers

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Abstract—Reaction of arylmethylidene derivatives of malononitrile dimer with 1,3-cyclohexanediones in anhydrous methanol in the presence of sodium methylate as catalyst affords 4-amino-5-aryl-2-methoxy-6-oxo-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]naphthyridine-3-carbonitrile. In the presence of strong electron-donor substituents in the benzene ring the reaction takes another route resulting in 4-amino-2-aryl-6-methoxypyridine-3,5-dicarbonitriles.

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The interest to 1,8-naphthyridine derivatives is mainly due to the presence of their structural fragment in natural objects and to the fact that some of them exhibit antibacterial, antiphlogistic, antihypertensive, antiallergic, and the kinds of biologic action [1]. Specimens of this class are successfully applied as herbicides [2], drugs against memory failure [3], and antibiotics [4].

The classic procedures of 1,8-naphthyridine derivatives preparation are underlain by modified methods of Friedlaender, Knorr, Conrad–Limpach, Combes utilizing 2-aminopyridines as initial compounds [5]. Yet the synthesis of 1,8-naphthyridine polyfunctional derivatives by these approaches is often a laborious and multistage process [6].

Utilization of cascade reactions [7] may be an alternative way to derivatives of 1,8-naphthyridine. As known, this strategy makes it possible to convert the most completely the initial component into the final product, reduces the number of intermediate technologic stages, of auxiliary components, reduces the energy consumption, the toxicity of the process, leading finally to the implementation of the concepts of the "green chemistry" into the organic synthesis.

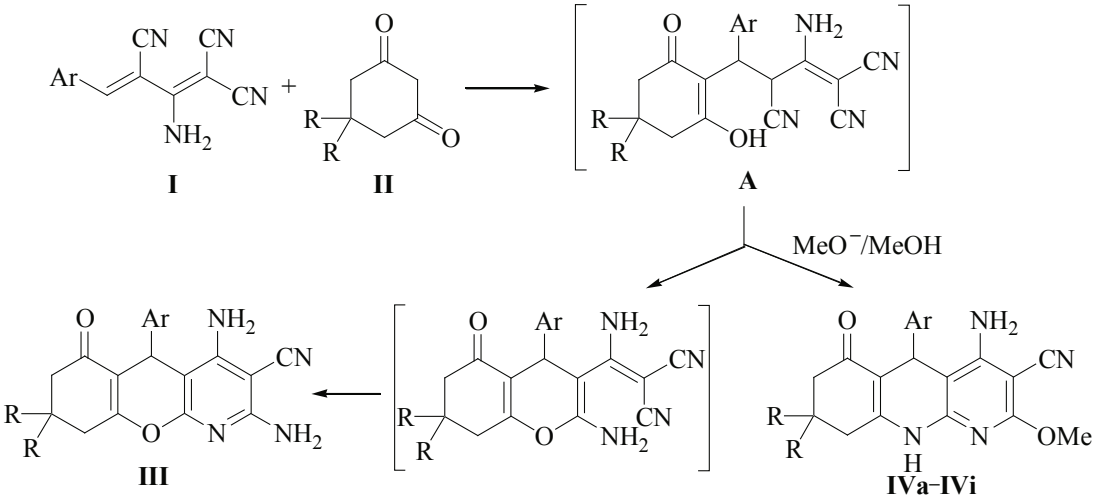
The necessary conditions for occurrence of such reactions is the presence in the reagents structure of several reactive sites of diverse character capable of participation in domino-processes. The formation of azaheterocycles, in particular, of fused ones, is favored by the presence in the structure of the initial compounds of several cyano groups since the latter are able to be involved in the cascade processes of heterocyclization under the action of nucleophilic reagents.

Arylmethylidene derivatives of malononitrile dimer **I** are promising substrates for the synthesis of heterocyclic compounds by cascade processes [8, 9]. This is caused by the presence in the structure of such compounds along with the system of conjugated multiple bonds also of an amino group and of cyano groups in various functional surrounding thus providing possibilities for involving them into intramolecular heterocyclization.

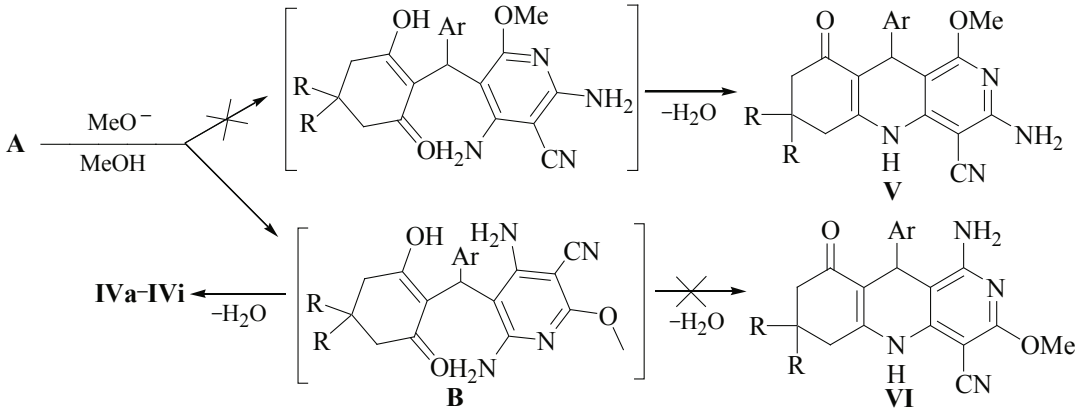
We formerly published the results of the reaction of compounds **I** with dimedone (**II**) [10]. As a result of the addition of the methylene-active compound along Michael reaction and of a series of intramolecular processes we obtained 5*H*-chromeno[2,3-*b*]pyridine derivatives **III** (Scheme 1).

The key stage of this process is evidently the intramolecular nucleophilic addition of the hydroxy group from the Michael adduct **A** to the cyano group with the formation of a pyran ring. The alternative course when the keto

Scheme 1.



Scheme 2.



R = H, Ar = Ph (**a**); R = Me, Ar = Ph (**b**), 4-MeC_6H_4 (**c**), 3,4-$(MeO)_2C_6H_3$ (**d**), 4-FC_6H_4 (**e**), 2-ClC_6H_4 (**f**), 3-BrC_6H_4 (**g**), 3,4-$Cl_2C_6H_3$ (**h**), 2-thienyl (**i**).

form of the adduct enters the reaction to provide a pyridine ring does not occur. In anhydrous methanol with sodium methylate as catalyst we succeeded in changing the reaction direction and as a result we obtained in 80–98% yields 4-amino-5-aryl-2-methoxy-6-oxo-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]naphthyridine-3-carbonitriles **IVa–IVi** (Scheme 2).

Evidently after the formation of Michael adduct **A** a nucleophilic addition occurs of methanol to a cyano group affording pyridine derivative **B**. The formation of compounds **IVa–IVi** is completed by the intramolecular condensation involving the keto group and the α-amino group of pyridine. Although the suggested sequence of transformations may include two alternative cyclization versions with the participation of the γ-amino group to give compounds **V, VI**, the NMR spectra NOESY and HMBC indicate the formation of compounds **IVa–IVi**.

The NOESY spectrum of compound **IVa** shows that the protons of amino group (6.42 ppm) correlate with the proton contiguous to the phenyl substituent (5.17 ppm) and the *ortho*-protons of the benzene ring (7.27 ppm), indicating their spatial proximity (Fig. 1) and unambiguously excluding the formation of compound **V**.

In the HMBC spectrum of compound **IVg** on the line of the chemical shift of the proton near the aryl substituent (5.18 ppm) correlation peaks appear corresponding to the scaffold atoms C^4 (149.49 ppm), C^{4a} (95.40 ppm), C^{5a} (108.97 ppm), C^6 (193.40 ppm), C^{9a} (151.34 ppm), C^{10a}

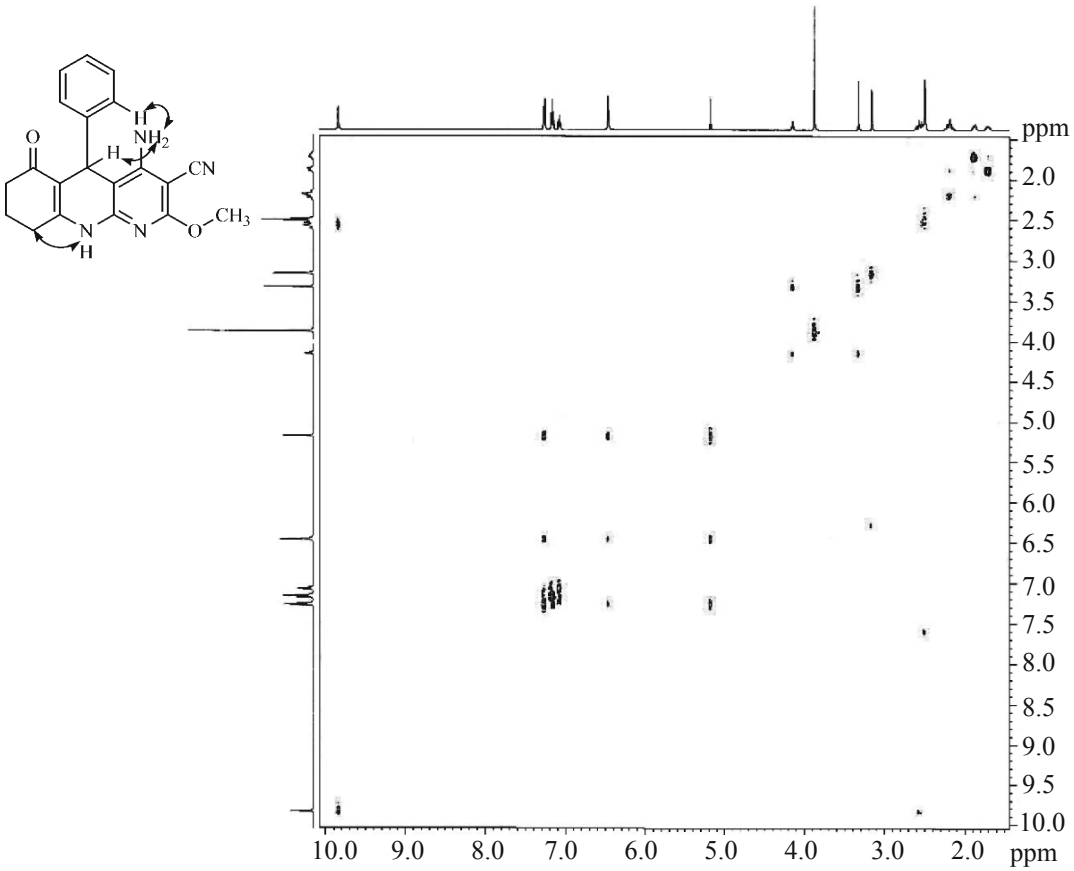


Fig. 1. NOESY NMR spectrum of 4-amino-2-methoxy-6-oxo-5-phenyl-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]naphthyridine-3-carbonitrile (**IVa**).

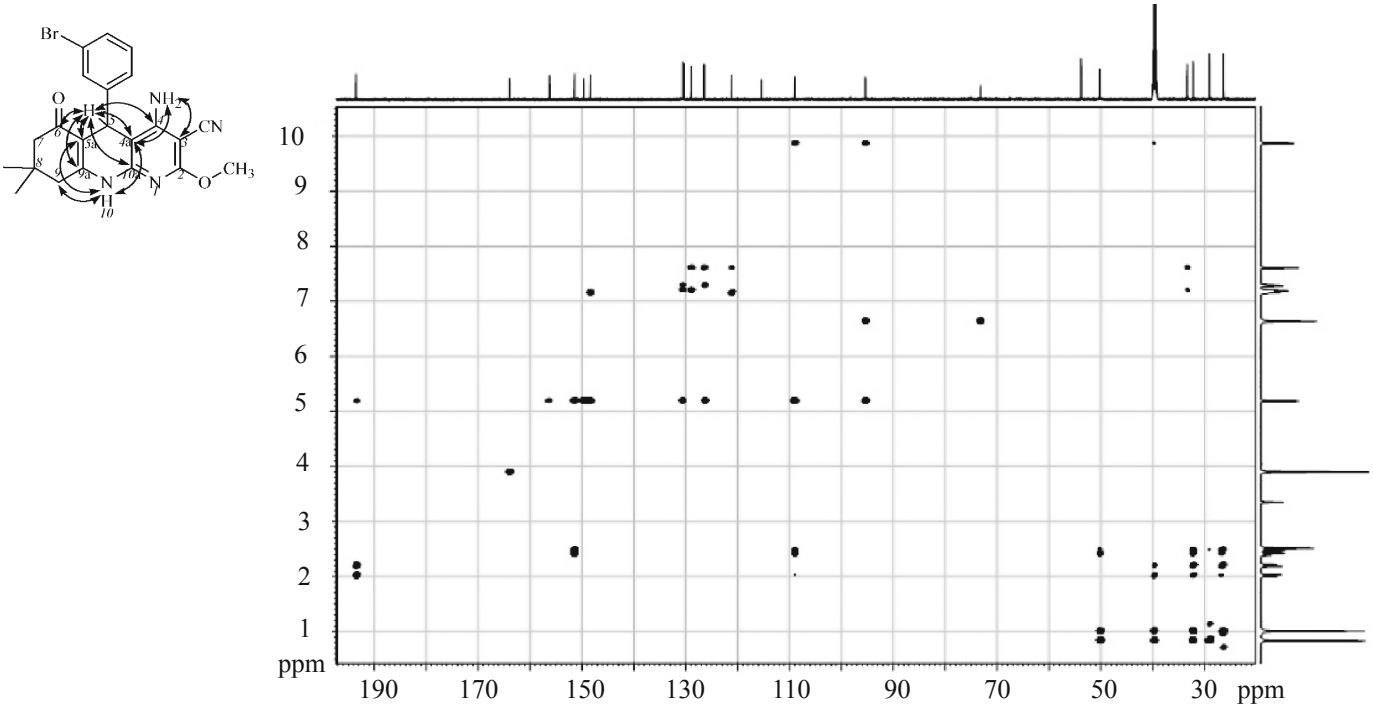
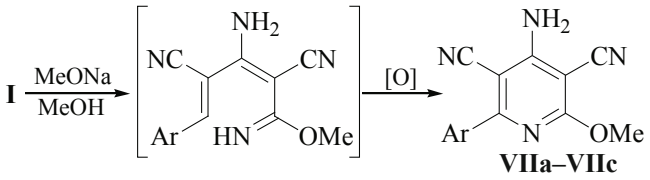


Fig. 2. HMBC NMR spectrum of 4-amino-5-(3-bromophenyl)-2-methoxy-8,8-dimethyl-6-oxo-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]naphthyridine-3-carbonitrile (**IVg**).

(156.35 ppm), and of carbon atoms of the aryl substituent (Fig. 2). The chemical shift of the protons of amino group (6.63 ppm) correlates with the shifts of atoms C^3 (73.19 ppm), C^{4a} (95.40 ppm) of the naphthyridine fragment excluding the possibility of structure **VI** formation for in the latter no correlation should occur between the amino group protons and the carbon atom bearing the cyano group. Besides, in compound **VI** this atom should correlate with the NH proton (9.86 ppm), and this peak does not exist in the spectrum. Instead on the line of the chemical shift of the NH proton the correlation peaks are observed at the coordinates of atoms C^{4a} (95.40 ppm), C^{5a} (108.97 ppm) and C^9 (39.77 ppm). The coordination peaks observed in the HMBC spectrum in the coordinates of the chemical shifts of alkyl and aryl protons and carbon atoms once and for all confirm the formation of structure **IV**.

Analogous syntheses proceeding from *p*-dimethylaminophenyl-, *p*-hydroxyphenyl-, and 4-hydroxy-3-methoxyphenyl-substituted compounds **I** were unsuccessful, and we isolated in the course of the reaction 4-amino-2-aryl-6-methoxypyridine-3,5-dicarbonitriles **VIIa–VIIc** in 54–76% yields.



VIIa–VIIc

Ar = 4-$Me_2NC_6H_4$ (**a**), 4-HOC_6H_4 (**b**), 3-MeO-4-HOC_6H_3 (**c**).

This alternative reaction route originates apparently from the strong positive mesomeric effect from hydroxy- and *N*,*N*-dimethylamino groups leading to the deactivation of the double bond. As a result in the initial stage of the reaction instead of Michael addition a nucleophilic attack proceeds of alcoholate anion on the cyano group of the enaminodinitrile fragment with the subsequent formation of a dihydropyridine ring. The reaction was completed by the aromatization of the system through the deprotonation. The mechanism of the latter is not clear up till now, but the initial diketone **II** may act as an oxidizer. The structure of pyridine derivatives **VII** was proved by IR, ^1H, ^{13}C NMR, and mass spectra.

Thus we developed a simple and regiospecific synthesis of highly functionalized 1,8-naphthyridines applying the procedure of multicomponent cascade heterocyclization.

EXPERIMENTAL

The monitoring of reaction progress and checking the purity of compounds synthesized was performed by TLC on Silufol UV-254 plates (development by UV irradiation, in iodine vapor, and by thermal decomposition). IR spectra were recorded on an IR Fourier spectrophotometer FSM-1202 from mulls in mineral oil. ^1H and ^{13}C NMR spectra were registered on a spectrometer Bruker DRX-500 (500.13 and 125.76 MHz respectively) in DMSO-d_6, internal reference TMS. Mass spectra were taken on an instrument Finnigan MAT INCOS-50 (EI, 70 eV).

2-Amino-4-phenylbuta-1,3-diene-1,1,3-tricarbonitrile (Ia). A mixture of 0.106 g (1 mmol) of benzaldehyde, 0.132 g (1 mmol) of malonodinitrile dimer, and 0.00145 g (0.01 mmol) of piperidine acetate was stirred in 20 mL of ethanol at 65–70°C for 10 min (TLC monitoring). On cooling the separated precipitate was filtered off, washed with ethanol. Yield 2.16 g (98%), mp 220–221°C (decomp.) {223°C (decomp.) [8]}.

Compounds **Ib–Ik** were similarly obtained and were used in further syntheses without purification.

2-Amino-4-(p-tolyl)buta-1,3-diene-1,1,3-tricarbonitrile (Ib). Yield 87%, mp 239–240°C (decomp.).

2-Amino-4-(3,4-dimethoxyphenyl)buta-1,3-diene-1,1,3-tricarbonitrile (Ic). Yield 83%, mp 198–199°C (decomp.).

2-Amino-4-(4-fluorophenyl)buta-1,3-diene-1,1,3-tricarbonitrile (Id). Yield 96%, mp 197–198°C (decomp.).

2-Amino-4-(2-chlorophenyl)buta-1,3-diene-1,1,3-tricarbonitrile (Ie). Yield 93%, mp 199–200°C (decomp.).

2-Amino-4-(3-bromophenyl)buta-1,3-diene-1,1,3-tricarbonitrile (If). Yield 94%, mp 226–227°C (decomp.).

2-Amino-4-(3,4-dichlorophenyl)buta-1,3-diene-1,1,3-tricarbonitrile (Ig). Yield 98%, mp 233–235°C (decomp.).

2-Amino-4-(thiophen-2-yl)buta-1,3-diene-1,1,3-tricarbonitrile (Ih). Yield 78%, mp 229–230°C (decomp.).

2-Amino-4-[4-(dimethylamino)phenyl]buta-1,3-diene-1,1,3-tricarbonitrile (Ii). Yield 86%, mp 162–163°C (decomp.).

2-Amino-4-(4-hydroxyphenyl)buta-1,3-diene-1,1,3-tricarbonitrile (Ij). Yield 80%, mp 208–209°C (decomp.) {225°C (decomp.) [9]}.

2-Amino-4-(4-hydroxy-3-methoxyphenyl)buta-1,3-diene-1,1,3-tricarbonitrile (Ik). Yield 84%, mp 174–175°C (decomp.).

4-Amino-2-methoxy-6-oxo-5-phenyl-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]naphthyridine-3-carbonitrile (IVa). To a solution of 0.023 g (1 mmol) of sodium in 3 mL of anhydrous alcohol was added 0.112 g (1 mmol) of 1,3-cyclohexanedione, after its dissolution 0.22 g (1 mmol) of benzylidene derivative of malononitrile dimer **IIa** was added. The reaction mixture was refluxed for 0.5–1 h, cooled, neutralized with conc. HCl to pH 5–6, the separated precipitate was filtered off, washed with alcohol, and recrystallized from acetonitrile. Yield 0.31 g (90%), mp 301–302°C (decomp.). IR spectrum, ν, cm^{-1}: 3380 (NH_2), 3230 (NH), 2228 (C≡N), 1660 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.70–1.74 m (1H, CH_2CO), 1.87–1.90 m (1H, CH_2CO), 2.18–2.23 m (2H, CH_2), 3.29 s (2H, CH_2), 3.88 s (3H, OCH_3), 5.17 s (1H, CH), 6.42 s (2H, NH_2), 7.07 t (1H, C_6H_5, *J* 7.3 Hz), 7.17 t (2H, C_6H_5, *J* 7.3 Hz), 7.27 d (2H, C_6H_5, *J* 7.3 Hz), 9.79 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 20.81, 26.46 (C^7, C^8), 33.41 (C^5), 36.76 (C^9), 53.67 (OCH_3), 73.07 (C^3), 95.90 (C^{4a}), 110.76 (C^{5a}), 115.41 (CN), 126.06, 127.90, 127.53, 145.97 (C_6H_5), 149.63 (C^4), 152.94 (C^{9a}), 156.18 (C^{10a}), 163.73 (C^2), 193.76 (C=O). Mass spectrum, *m/z* (I_{rel}, %): 346 (32) $[M]^+$, 269 (100) $[M - 77]^+$. Found, %: C 69.39; H 5.26; N 16.15. $C_{20}H_{18}N_4O_2$. Calculated, %: C 69.35; H 5.24; N 16.17. *M* 346.14.

Compounds **IVb–IVi, VIIa–VIIc** were similarly prepared.

4-Amino-8,8-dimethyl-2-methoxy-6-oxo-5-phenyl-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]naphthyridine-3-carbonitrile (IVb). Yield 94%, mp 291–292°C (decomp.). IR spectrum, ν, cm^{-1}: 3400, 3370 (NH_2), 3240 (NH), 2230 (C≡N), 1658 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.82 s (3H, CH_3), 1.00 s (3H, CH_3), 1.98 d (1H, CH_2CO, *J* 16.1 Hz), 2.18 d (1H, CH_2CO, *J* 16.1 Hz), 2.38 d (1H, CH_2, *J* 17.3 Hz), 2.47 d (1H, CH_2, *J* 17.3 Hz), 3.88 s (3H, OCH_3), 5.15 s (1H, CH), 6.51 s (2H, NH_2), 7.08 t (1H, C_6H_5, *J* 7.3 Hz), 7.18 t (2H, C_6H_5, *J* 7.6 Hz), 7.29 d (2H, C_6H_5, *J* 7.3 Hz), 9.80 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 374 (12) $[M]^+$, 297 (100) $[M - 77]^+$. Found, %: C 70.60; H 5.89; N 14.93. $C_{22}H_{22}N_4O_2$. Calculated, %: C 70.57; H 5.92; N 14.96. *M* 374.17.

4-Amino-8,8-dimethyl-2-methoxy-6-oxo-5-(*p*-toluyl)-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]naphthyridine-3-carbonitrile (IVb). Yield 86%, mp 314–315°C (decomp.). IR spectrum, ν, cm^{-1}: 3433, 3372 (NH_2), 3232 (NH), 2241 (C≡N), 1652 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.82 s (3H, CH_3), 1.00 s (3H, CH_3), 1.98 d (1H, CH_2CO, *J* 16.5 Hz), 2.16 d (1H, CH_2CO, *J* 16.5 Hz), 2.18 s (3H, $C\underline{H}_3C_6H_4$), 2.38 d (1H, CH_2, *J* 17.0 Hz), 2.46 d (1H, CH_2, *J* 17.0 Hz), 3.87 s (3H, OCH_3), 5.10 s (1H, CH), 6.45 s (2H, NH_2), 6.97 d (2H, C_6H_4, *J* 8.1 Hz), 7.16 d (2H, C_6H_4, *J* 8.1 Hz), 9.79 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 388 (34) $[M]^+$, 297 (100) $[M - 91]^+$. Found, %: C 71.15; H 6.25; N 14.39. $C_{23}H_{24}N_4O_2$. Calculated, %: C 71.11; H 6.23; N 14.42. *M* 388.19.

4-Amino-5-(3,4-dimethoxyphenyl)-8,8-dimethyl-2-methoxy-6-oxo-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]naphthyridine-3-carbonitrile (IVd). Yield 80%, mp 188–189°C (decomp.). IR spectrum, ν, cm^{-1}: 3410, 3347 (NH_2), 3236 (NH), 2210 (C≡N), 1660 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.85 s (3H, CH_3), 1.00 s (3H, CH_3), 1.99 d (1H, CH_2CO, *J* 16.0 Hz), 2.19 d (1H, CH_2CO, *J* 16.0 Hz), 2.38 d (1H, CH_2, *J* 17.0 Hz), 2.47 d (1H, CH_2, *J* 17.0 Hz), 3.65 s (3H, $OCH_3C_6H_3$), 3.67 s (3H, $OCH_3C_6H_3$), 3.87 s (3H, OCH_3), 5.07 s (1H, CH), 6.51 s (2H, NH_2), 6.66 dd (1H, C_6H_3, *J* 2.1, 8.3 Hz), 6.75 d (1H, C_6H_3, *J* 8.3 Hz), 7.07 d (1H, C_6H_3, *J* 2.1 Hz), 9.75 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 434 (22) $[M]^+$, 297 (100) $[M - 137]^+$. Found, %: C 66.38; H 6.00; N 12.88. $C_{24}H_{26}N_4O_4$. Calculated, %: C 66.34; H 6.03; N 12.89. *M* 434.20.

4-Amino-8,8-dimethyl-2-methoxy-6-oxo-5-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]-naphthyridine-3-carbonitrile (IVe). Yield 91%, mp 263–264°C (decomp.). IR spectrum, ν, cm^{-1}: 3457, 3387 (NH_2), 3236 (NH), 2216 (C≡N), 1692 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.80 s (3H, CH_3), 1.00 s (3H, CH_3), 1.98 d (1H, CH_2CO, *J* 16.0 Hz), 2.18 d (1H, CH_2CO, *J* 16.0 Hz), 2.37 d (1H, CH_2, *J* 17.1 Hz), 2.47 d (1H, CH_2, *J* 17.1 Hz), 3.88 s (3H, OCH_3), 5.17 s (1H, CH), 6.55 s (2H, NH_2), 7.00 t (2H, C_6H_4, *J* 8.9 Hz), 7.30 d.d (2H, C_6H_4, *J* 2.5, 6.1 Hz), 9.82 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 392 (21) $[M]^+$, 297 (100) $[M - 95]^+$, 245 (22) $[M - 147]^+$. Found, %: C 67.35; H 5.36; N 14.25. $C_{22}H_{21}FN_4O_2$. Calculated, %: C 67.33; H 5.39; N 14.28. *M* 392.16.

4-Amino-8,8-dimethyl-2-methoxy-6-oxo-5-(2-chlorophenyl)-5,6,7,8,9,10-hexahydrobenzo[*b*]-[1,8]-naphthyridine-3-carbonitrile (IVf). Yield 96%, mp 304–305°C (decomp.). IR spectrum, ν, cm^{-1}: 3468, 3349 (NH_2), 3247 (NH), 2210 (C≡N), 1646 (C=O).

^{1}H NMR spectrum, δ, ppm: 0.86 s (3H, CH_3), 1.00 s (3H, CH_3), 1.94 d (1H, CH_2CO, *J* 16.2 Hz), 2.16 d (1H, CH_2CO, *J* 16.2 Hz), 2.40 d (1H, CH_2, *J* 16.7 Hz), 2.49 d (1H, CH_2, *J* 16.7 Hz), 3.88 s (3H, OCH_3), 5.25 s (1H, CH), 6.10 s (2H, NH_2), 7.15 d.t (1H, C_6H_4, *J* 1.6, 7.6 Hz), 7.23 d.t (1H, C_6H_4, *J* 1.3, 7.6 Hz), 7.30 d.d (1H, C_6H_4, *J* 1.2, 7.9 Hz), 7.45 d.d (1H, C_6H_4, *J* 1.5, 7.8 Hz), 9.95 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 410 (6) $[M]^+$, 408 (17) $[M]^+$, 297 (100) $[M - 111]^+$. Found, %: C 64.63; H 5.16; N 13.68. $C_{22}H_{21}ClN_4O_2$. Calculated, %: C 64.62; H 5.18; N 13.70. *M* 408.14.

4-Amino-5-(3-bromophenyl)-2-methoxy-8,8-dimethyl-6-oxo-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]-naphthyridine-3-carbonitrile (IVg). Yield 98%, mp 248–249°C (decomp.). IR spectrum, ν, cm^{-1}: 3411, 3350 (NH_2), 3242 (NH), 2210 (C≡N), 1659 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.82 s (3H, CH_3), 1.00 s (3H, CH_3), 2.00 d (1H, CH_2CO, *J* 16.3 Hz), 2.19 d (1H, CH_2CO, *J* 16.3 Hz), 2.39 d (1H, CH_2, *J* 17.2 Hz), 2.48 d (1H, CH_2, *J* 17.2 Hz), 3.89 s (3H, OCH_3), 5.18 s (1H, CH), 6.63 s (2H, NH_2), 7.16 t (1H, C_6H_4, *J* 7.7 Hz), 7.19 d.t (1H, C_6H_4, *J* 1.4, 7.7 Hz), 7.28 d.t (1H, C_6H_4, *J* 1.7, 7.6 Hz), 7.60 t (1H, C_6H_4, *J* 1.7 Hz), 9.86 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 454 (6) $[M]^+$, 453 (2) $[M]^+$, 452 (6) $[M]^+$, 297 (100) $[M - 155]^+$. Found, %: C 58.25; H 4.64; N 12.33. $C_{22}H_{21}BrN_4O_2$. Calculated, %: C 58.29; H 4.67; N 12.36. *M* 452.08.

4-Amino-5-(3,4-dichlorophenyl)-8,8-dimethyl-2-methoxy-6-oxo-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]-naphthyridine-3-carbonitrile (IVh). Yield 97%, mp 277–278°C (decomp.). IR spectrum, ν, cm^{-1}: 3412, 3343 (NH_2), 3242 (NH), 2208 (C≡N), 1654 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.81 s (3H, CH_3), 1.00 s (3H, CH_3), 2.00 d (1H, CH_2CO, *J* 16.1 Hz), 2.19 d (1H, CH_2CO, *J* 16.1 Hz), 2.39 d (1H, CH_2, *J* 17.2 Hz), 2.48 d (1H, CH_2, *J* 17.2 Hz), 3.89 s (3H, OCH_3), 5.20 s (1H, CH), 6.66 s (2H, NH_2), 7.14 d.d (1H, C_6H_3, *J* 2.0, 8.4 Hz), 7.46 d (1H, C_6H_3, *J* 8.4 Hz), 7.66 d (1H, C_6H_3, *J* 2.0 Hz), 9.91 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 444 (1) $[M]^+$, 442 (3) $[M]^+$, 297 (100) $[M - 145]^+$. Found, %: C 59.58; H 4.53; N 12.66. $C_{22}H_{20}Cl_2N_4O_2$. Calculated, %: C 59.60; H 4.55; N 12.64. *M* 442.10.

4-Amino-8,8-dimethyl-2-methoxy-6-oxo-5-(2-thienyl)-5,6,7,8,9,10-hexahydrobenzo[*b*][1,8]naphthyridine-3-carbonitrile (IVi). Yield 93%, mp 311–312°C (decomp.). IR spectrum, ν, cm^{-1}: 3412, 3343 (NH_2), 3242 (NH), 2208 (C≡N), 1654 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.91 s (3H, CH_3), 1.01 s (3H, CH_3), 2.06 d (1H, CH_2CO, *J* 16.3 Hz), 2.23 d (1H, CH_2CO, *J* 16.3 Hz), 2.38 d (1H, CH_2, *J* 17.4 Hz), 2.47 d (1H, CH_2, *J* 17.4 Hz), 3.88 s (3H, OCH_3), 5.54 s (1H, CH), 6.74 s (2H, NH_2), 6.80 d.d (1H, C_4H_3S, *J* 3.3, 5.0 Hz), 6.84 d (1H, C_4H_3S, *J* 3.3 Hz), 7.17 d.d (1H, C_4H_3S, *J* 1.2, 5.0 Hz), 9.89 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 380 (53) $[M]^+$, 297 (100) $[M - 83]^+$. Found, %: C 63.10; H 5.32; N 14.75. $C_{20}H_{20}N_4O_2S$. Calculated, %: C 63.14; H 5.30; N 14.73. *M* 380.13.

4-Amino-2-[4-(dimethylamino)phenyl]-6-methoxypyridine-3,5-dicarbonitrile (VIIa). Yield 68%, mp 258–259°C (decomp.). IR spectrum, ν, cm^{-1}: 3343, 3237 (NH_2), 2206 (C≡N). ^{1}H NMR spectrum, δ, ppm: 3.02 s [6H, $(CH_3)_2N$], 4.00 s (3H, OCH_3), 6.80 d (2H, C_6H_4, *J* 9.0 Hz), 7.49 s (2H, NH_2), 7.86 d (2H, C_6H_4, *J* 9.0 Hz). ^{13}C NMR spectrum, δ, ppm: 54.47 (OCH_3), 74.62, 84.20 ($C^{3,5}$), 113.88, 116.59 (CN), 111.06, 123.15, 130.29, 152.11 (C_6H_4), 159.83, 162.76, 165.50 ($C^{2,4,6}$). Mass spectrum, *m/z* (I_{rel}, %): 293 (100) $[M]^+$, 249 (5) $[M - 44]^+$. Found, %: C 65.55; H 5.19; N 23.86. $C_{16}H_{15}N_5O$. Calculated, %: C 65.52; H 5.15; N 23.88. *M* 293.13.

4-Amino-2-(4-hydroxyphenyl)-6-methoxypyridine-3,5-dicarbonitrile (VIIb) was purified by column chromatography. Yield 54%, mp 268–269°C (decomp.). IR spectrum, ν, cm^{-1}: 3348, 3240 (NH_2), 2224 (C≡N). ^{1}H NMR spectrum, δ, ppm: 4.00 s (3H, OCH_3), 6.90 d (2H, C_6H_4, *J* 8.7 Hz), 7.56 s (2H, NH_2), 7.79 d (2H, C_6H_4, *J* 8.7 Hz), 10.13 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 266 (100) $[M]^+$, 249 (11) $[M - 17]^+$, 235 (21) $[M - 31]^+$. Found, %: C 63.16; H 3.82; N 21.06. $C_{14}H_{10}N_4O_2$. Calculated, %: C 63.15; H 3.79; N 21.04. *M* 266.08.

4-Amino-2-(4-hydroxy-3-methoxyphenyl)-6-methoxypyridine-3,5-dicarbonitrile (VIIc). Yield 76%, mp 266–267°C (decomp.). IR spectrum, ν, cm^{-1}: 3377, 3243 (NH_2), 2224 (C≡N). ^{1}H NMR spectrum, δ, ppm: 3.83 s (3H, 3-C$\underline{H}_3$O), 4.02 s (3H, 6-CH_3O), 6.92 d (1H, C_6H_3, *J* 8.3 Hz), 7.43 d.d (1H, C_6H_3, *J* 2.1, 8.3 Hz), 7.51 d (1H, C_6H_3, *J* 2.1 Hz), 7.57 s (2H, NH_2), 9.76 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 296 (44) $[M]^+$. Found, %: C 60.85; H 4.06; N 18.93. $C_{15}H_{12}N_4O_3$. Calculated, %: C 60.81; H 4.08; N 18.91. *M* 296.09.

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