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ORIGINAL PAPER

Three-component synthesis of some 2-amino-5-hydroxy-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carbonitriles and 2-(cyanoamino)-4-hydroxypyrimidine-5-carbonitriles

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Abstract Nine new 2-amino-5-hydroxy-[1,2,4]triazolo-[1,5-*a*]pyrimidine-6-carbonitriles and eight 2-(cyanoamino)-4-hydroxypyrimidine-5-carbonitriles have been synthesized in a simple and convenient method by three-component condensation of aromatic aldehydes, ethyl cyanoacetate, and 3,5-diamino-1,2,4-triazole or cyanoguanidine hydrochloride in alkaline ethanol. All new synthesized compounds were characterized by nuclear magnetic resonance (NMR), infrared (IR), ultraviolet (UV), mass spectrometry (MS), and elemental analyses.

Keywords Triazolopyrimidine · Pyrimidine · Aldehyde · Three-component synthesis · Triazole

Introduction

Fused triazole and pyrimidine ring systems have been an interesting topic in the fields of medicinal and agricultural chemistry for many years [1, 2]. Among their important effects, some triazolopyrimidine derivatives are known as dual thrombin/factor Xa inhibitors [3], blood pressure regulators [4], antibacterial agents [5], human adenosine A2a and A3 receptor ligands [6], and cardiovascular vasodilators [7]. Additionally, many triazolopyrimidine-2-sulfonamide derivatives, such as florasulam, flumetsulam, and metosulam, are commercially available as acetolactate synthase-inhibiting herbicides [8, 9]. Recently some new substituted pyrimidine derivatives have been synthesized, which exhibit analgesic, anti-inflammatory, antiparkinsonian, and androgenic–anabolic activities [10–12].

It is well known that multicomponent reactions (MCR) consisting of two or more synthetic steps, which are carried out without isolation of any intermediate, allow to reduce time and save money, energy, and raw materials. Also, the development of simple synthetic routes for widely used organic compounds from readily available reagents is one of the major tasks in organic synthesis.

Many literature reports concerning the synthesis of systems incorporating a triazolopyrimidine moiety [13] either start from reaction of hydrazine with an acid derivative (orthoformate [14] or activated acids [15]) or via oxidative cyclization of a hydrazone with reagents such as N-Bromosuccinimide (NBS) [16], lithium iodide or sodium carbonate [17], $Pb(OAc)_4$ [18], $FeCl_3$ [19], and iodobenzene diacetate [20].

In this paper, we report the first synthesis of some amino derivatives of triazolopyrimidine by three-component condensation of aromatic aldehydes, ethyl cyanoacetate, and 3,5-diamino-1,2,4-triazole in alkaline ethanol.

Results and discussion

One of the most widely used routes for preparation of 2-amino-1,2,4-triazolo[1,5-*a*]pyrimidines is cyclocondensation of 3,5-diamino-1,2,4-triazole with unsaturated aldehydes and ketones followed by heteroaromatization of the resulting 2-amino-4,7-dihydro-[1,2,4]triazolo[1,5-*a*]pyrimidines [21, 22]. There is no report concerning one-pot synthesis of 2-amino-[1,2,4]triazolopyrimidine compounds using aromatic aldehydes, ethyl cyanoacetate, and 3,5-diamino-1,2,4-triazole. Of course synthesis of 2-amino-6-hydroxy-4-arylpyrimidine-5-carbonitriles has been developed by three-component condensation of aromatic aldehydes, ethyl

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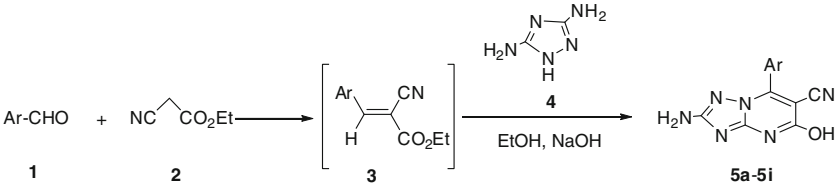
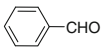
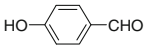
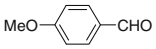
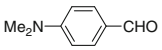
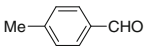
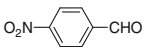
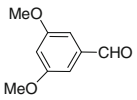
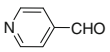
Table 1 Synthesis of 2-amino-[1,2,4]triazolopyrimidine derivatives



Product	Aldehyde	Time (min)	Yield (%)
5a		180	85
5b		145	83
5c		140	89
5d		150	91
5e		140	92
5f		160	93
5g		160	90
5h		140	90
5i		160	92

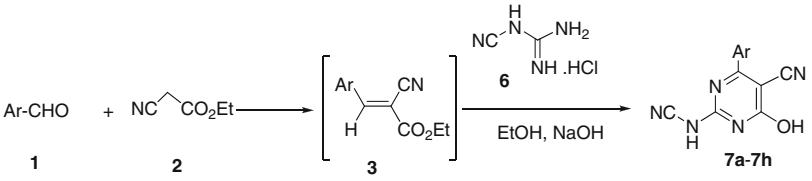
cyanoacetate, and guanidine hydrochloride [23]. The target products **5a–5i** were synthesized by a three-component condensation procedure as shown in Table 1. Firstly, the aromatic aldehyde **1** reacted with ethyl cyanoacetate (**2**) to afford intermediate **3**, which cyclized with 3,5-diamino-1,2,4-triazole (**4**) to give 2-amino-[1,2,4]triazolopyrimidines **5a–5i**. The formation of the products **5a–5i** is assumed to take place via an initial addition of the more nucleophilic endocyclic nitrogen in 3,5-diamino-1,2,4-triazole to the intermediate **3** with subsequent intramolecular cyclization and aromatization to give the final products **5a–5i**, adapting a mechanism postulated by Shaaban [24]. The method exploited works well with a variety of aromatic aldehydes as well as heteroaromatic aldehydes to afford corresponding 2-amino-[1,2,4]triazolopyrimidine derivatives in excellent yields (Table 1). We reasoned that electron-donating as well as electron-withdrawing groups present in aryl aldehydes do not alter the theme of the method in terms of yield. The mass spectrum of compound **5a**, taken as an example of the prepared series, revealed a molecular ion peak at $m/z = 252$. Its ^{1}H NMR spectrum revealed a broad singlet signal at $\delta = 3.4$ ppm due to NH_2 protons and multiple signals at $\delta = 6.9$–7.9 ppm due to phenyl protons, in addition to a singlet signal at 13.1 ppm due to the OH proton. With this encouraging result in hand, we attempted the synthesis of some 2-(cyanoamino)-4-hydroxypyrimidine-5-carbonitrile compounds. Products **7a–7h** were synthesized by a three-component condensation procedure as shown in Table 2. Firstly, the aromatic aldehyde **1** reacted with ethyl cyanoacetate (**2**) to afford intermediate **3**, which cyclized with cyanoguanidine hydrochloride (**6**) to give 2-(cyanoamino)-4-hydroxypyrimidine-5-carbonitriles **7a–7h**.

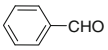
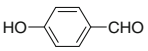
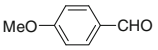
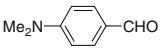
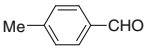
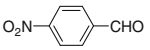
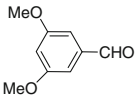
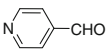
We used a series of aromatic and heteroaromatic aldehydes having electron-donating as well as electron-withdrawing substituents to obtain the corresponding 2-(cyanoamino)-4-hydroxypyrimidine-5-carbonitriles (Table 2). As can be seen from Table 2, when aromatic aldehydes containing electron-donating groups were employed, a longer reaction time was required than those of electron-withdrawing groups on aromatic rings. The structures of all compounds were characterized by ^{1}H NMR, ^{13}C NMR, IR, MS, and elemental analyses.

Conclusion

Herein we report synthesis of several new 2-amino-5-hydroxy[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carbonitriles **5a–5i** and 2-(cyanoamino)-4-hydroxypyrimidine-5-carbonitriles **7a–7h** via a simple and convenient method by three-component condensation of aromatic aldehydes, ethyl cyanoacetate, and 3,5-diamino-1,2,4-triazole or cyanoguanidine hydrochloride, respectively, in alkaline ethanol. The method exploited works well with a variety of aromatic aldehydes as well as heteroaromatic aldehydes to afford corresponding triazolopyrimidine and pyrimidine

Table 2 Synthesis of 2-(cyanoamino)-4-hydroxypyrimidine-5-carbonitriles



Product	Aldehyde	Time (min)	Yield (%)
7a		150	89
7b		160	85
7c		158	81
7d		160	78
7e		155	75
7f		140	83
7g		150	85
7h		148	86

cyanamide derivatives in excellent yields (Tables 1, 2). Electron-donating as well as electron-withdrawing groups present in aryl aldehydes do not alter the theme of the method in terms of yield.

Experimental

All reagents and solvents were purchased from Merck and Aldrich and used without further purification. The reactions were carried out under an atmosphere of air unless otherwise specified. The elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer, and results agreed with calculated values. ^{1}H NMR spectra were recorded at 500 MHz and ^{13}C NMR spectra at 125 MHz on a Bruker spectrometer. Chemical shifts are reported in ppm relative to tetramethylsilane as internal standard. Mass spectra were taken by a Micromass Platform II in electrospray ionization (EI) mode (70 eV). Silica plates (Merck) were used for thin-layer chromatography (TLC) analysis.

General procedure for the synthesis of triazolopyrimidine derivatives

Aromatic aldehyde (10 mmol) and ethyl cyanoacetate (10 mmol) were added to 6 cm^3 2 M NaOH solution in 25 cm^3 ethanol. The mixture was stirred mechanically for 15 min, then 3,5-diamino-1,2,4-triazole (10 mmol) was added and the reaction mixture was refluxed until completion of reaction as monitored by TLC. After reaction completion (140–180 min), the reaction mixture was poured into iced water and neutralized by HCl (1:1) to get the desired product. The separated solid was filtered and washed with little distilled water to remove acid. Finally, the crude product was purified by recrystallization from ethanol to get pure product in almost quantitative yield.

2-Amino-5-hydroxy-7-phenyl[1,2,4]triazolo[1,5-a]-pyrimidine-6-carbonitrile (**5a**, $C_{12}H_8N_6O$)
White solid; m.p.: 182–184 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,360, 3,310, 2,831, 2,229, 1,721, 1,583, 1,559, 1,460, 1,428, 1,262, 806 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 420, 410, 265 nm; ^{1}H NMR ($CDCl_3$): δ = 3.9 (bs, 2H, NH_2), 6.91–7.92 (m, 5H, Ar–H), 13.11 (bs, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 94.31, 112.61, 117.81, 118.53, 134.40, 148.13, 151.34, 153.47, 153.72, 164.75 ppm; MS (EI): *m*/*z* = 252 (M^+), 225, 175, 147.

2-Amino-5-hydroxy-7-(4-hydroxyphenyl)[1,2,4]triazolo-[1,5-a]pyrimidine-6-carbonitrile (**5b**, $C_{12}H_8N_6O_2$)
Yellow solid; m.p.: 192–194 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,341, 3,315, 2,842, 2,230, 1,625, 1,589, 1,568, 1,462, 1,425, 1,232, 805 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 415, 413, 260 nm; ^{1}H NMR ($CDCl_3$): δ = 3.30 (bs, 2H, NH_2), 3.51 (bs, 1H, OH), 7.16 (d, *J* = 9.1 Hz, 2H, Ar–H), 7.15 (d, *J* = 9.1 Hz, 2H, Ar–H), 8.75 (bs, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 96.22, 113.63, 116.56, 122.93, 133.63, 147.00, 150.31, 152.49, 166.03, 166.71 ppm; MS (EI): *m*/*z* = 268 (M^+), 242, 191, 165.

2-Amino-5-hydroxy-7-(4-methoxyphenyl)[1,2,4]-triazolo[1,5-a]pyrimidine-6-carbonitrile
(**5c**, $C_{13}H_{10}N_6O_2$)
White solid; m.p.: 102–104 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,345, 3,321, 2,835, 2,227, 1,740, 1,585, 1,567, 1,471, 1,452, 1,244, 802 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 421, 417, 250 nm; ^{1}H NMR ($CDCl_3$): δ = 3.83 (bs, 2H, NH_2), 3.85 (s, 3H, CH_3), 7.14 (d, J = 8.9 Hz, 2H, Ar–H), 8.06 (d, J = 8.9 Hz, 2H, Ar–H), 8.30 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 53.73, 98.24, 114.94, 116.18, 123.90, 133.50, 145.13, 154.53, 155.41, 162.85, 163.56 ppm; MS (EI): m/z = 282 (M^+), 252, 227, 211, 135.

2-Amino-7-(4-(dimethylamino)phenyl)-5-hydroxy-[1,2,4]triazolo[1,5-a]pyrimidine-6-carbonitrile
(**5d**, $C_{14}H_{13}N_7O$)
Yellow solid; m.p.: 225–226 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,361, 3,318, 2,830, 2,230, 1,716, 1,582, 1,562, 1,459, 1,450, 1,231, 800 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 426, 411, 256 nm; ^{1}H NMR ($CDCl_3$): δ = 3.06 (s, 6H, CH_3), 3.31 (bs, 2H, NH_2), 6.81 (d, J = 9.1 Hz, 2H, Ar–H), 7.92 (d, J = 9.1 Hz, 2H, Ar–H), 13.27 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 42.12, 96.21, 111.64, 117.88, 118.39, 133.43, 133.50, 142.16, 148.73, 153.47, 153.72, 164.75 ppm; MS (EI): m/z = 295 (M^+), 279, 270, 252, 176, 151, 135.

2-Amino-5-hydroxy-7-(4-methylphenyl)[1,2,4]triazolo-[1,5-a]pyrimidine-6-carbonitrile (**5e**, $C_{13}H_{10}N_6O$)
White solid; m.p.: 234–235 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,352, 3,323, 2,228, 1,700, 1,574, 1,559, 1,449, 1,445, 1,237, 814 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 413, 410, 242 nm; ^{1}H NMR ($CDCl_3$): δ = 2.21 (s, 3H, CH_3), 3.51 (bs, 2H, NH_2), 7.01 (d, J = 8.2 Hz, 2H, Ar–H), 7.98 (d, J = 8.2 Hz, 2H, Ar–H), 12.21 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 43.12, 93.40, 112.16, 117.81, 119.23, 132.85, 133.17, 140.20, 148.13, 151.79, 152.74, 165.83 ppm; MS (EI): m/z = 266 (M^+), 252, 250, 241, 176, 151, 135.

2-Amino-5-hydroxy-7-(4-nitrophenyl)[1,2,4]-triazolo[1,5-a]pyrimidine-6-carbonitrile
(**5f**, $C_{12}H_7N_7O_3$)
Brown solid; m.p.: 160–163 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,355, 3,319, 2,815, 2,233, 1,710, 1,579, 1,562, 1,450, 1,447, 1,231, 804 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 417, 415, 248 nm; ^{1}H NMR ($CDCl_3$): δ = 3.12 (bs, 2H, NH_2), 7.21 (d, J = 8.6 Hz, 2H, Ar–H), 8.09 (d, J = 8.6 Hz, 2H, Ar–H), 11.01 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 95.42, 112.19, 116.57, 119.24, 133.81, 134.46, 140.55, 147.18, 150.93, 152.63, 166.43 ppm; MS (EI): m/z = 297 (M^+), 281, 272, 252, 176, 151, 135.

2-Amino-7-(3,5-dimethoxyphenyl)-5-hydroxy[1,2,4]-triazolo[1,5-a]pyrimidine-6-carbonitrile
(**5g**, $C_{14}H_{12}N_6O_3$)
Brown solid; m.p.: 172–175 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,349, 3,310, 2,838, 2,222, 1,708, 1,580, 1,566, 1,452, 1,448, 1,220, 825 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 421, 410, 241 nm; ^{1}H NMR ($CDCl_3$): δ = 3.80 (s, 3H, CH_3), 3.81 (s, 3H, CH_3), 3.28 (bs, 2H, NH_2), 6.09 (s, 1H, Ar–H), 8.02 (s, 2H, Ar–H), 9.22 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 54.12, 55.09, 98.58, 114.23, 117.35, 123.04, 133.92, 135.43, 148.27, 151.13, 153.60, 167.12 ppm; MS (EI): m/z = 312 (M^+), 287, 282, 252, 176.

2-Amino-5-hydroxy-7-(4-pyridyl)[1,2,4]-triazolo[1,5-a]pyrimidine-6-carbonitrile
(**5h**, $C_{11}H_7N_7O$)
Yellow solid; m.p.: 229–231 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,347, 3,316, 2,840, 2,214, 1,702, 1,586, 1,583, 1,450, 1,443, 1,271, 815 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 426, 407, 246 nm; ^{1}H NMR ($CDCl_3$): δ = 3.41 (bs, 2H, NH_2), 7.41 (d, J = 8.2 Hz, 2H, Py-H), 8.23 (d, J = 8.2 Hz, 2H, Py-H), 9.81 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 97.23, 113.27, 118.31, 122.63, 132.25, 147.20, 152.62, 155.61, 168.44 ppm; MS (EI): m/z = 253 (M^+), 228, 229, 176.

2-Amino-5-hydroxy-7-(2-thienyl)[1,2,4]triazolo-[1,5-a]pyrimidine-6-carbonitrile (**5i**, $C_{10}H_6N_6OS$)
Red solid; m.p.: 229–231 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,340, 3,320, 2,218, 1,717, 1,580, 1,575, 1,430, 1,449, 1,201, 805 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 416, 410, 241 nm; ^{1}H NMR ($CDCl_3$): δ = 3.55 (bs, 2H, NH_2), 7.34 (dd, J = 8.2, 7.3 Hz, 1H, Th–H), 8.05 (d, J = 8.2 Hz, 1H, Th–H), 8.20 (d, J = 7.3 Hz, 1H, Th–H), 9.81 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 97.50, 116.79, 128.68, 128.83, 135.49, 137.17, 139.36, 140.25, 147.77, 162.61 ppm; MS (EI): m/z = 258 (M^+), 228, 229, 176.

General procedure for the synthesis of (cyanoamino) pyrimidine derivatives

Aromatic aldehyde (10 mmol) and ethyl cyanoacetate (10 mmol) were added to 6 cm^3 2 M NaOH solution in 25 cm^3 ethanol. The mixture was stirred mechanically for 15 min, then cyanoguanidine hydrochloride (10 mmol) was added and the reaction mixture was refluxed until completion of reaction as monitored by TLC. After reaction completion (140–160 min), the reaction mixture was poured into iced water and neutralized by HCl (1:1) to get

the desired product. The separated solid was filtered and washed with little distilled water to remove acid. Finally, the crude product was purified by recrystallization from ethanol to get pure product in almost quantitative yield.

2-(Cyanoamino)-4-hydroxy-6-phenylpyrimidine-5-carbonitrile (**7a**, $C_{12}H_7N_5O$)
White solid; m.p.: 120–122 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,342, 3,319, 2,232, 1,705, 1,575, 1,566, 1,420, 1,410, 822 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 375, 252 nm; ^{1}H NMR ($CDCl_3$): δ = 4.13 (bs, 1H, NH), 7.01–8.02 (m, 5H, Ar–H), 8.43 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 94.11, 112.24, 116.60, 118.35, 134.81, 136.35, 152.74, 153.04, 147.77, 164.56 ppm; MS (EI): *m*/*z* = 237 (M^+), 212, 197, 161, 96.

2-(Cyanoamino)-4-hydroxy-6-(4-hydroxyphenyl)-pyrimidine-5-carbonitrile (**7b**, $C_{12}H_7N_5O_2$)
White solid; m.p.: 166–168 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,432, 3,220, 2,905, 2,247, 1,715, 1,676, 1,575, 1,566, 1,432, 1,420, 834 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 382, 262 nm; ^{1}H NMR ($CDCl_3$): δ = 3.70 (s, 1H, NH), 4.52 (s, 1H, OH), 6.89 (d, *J* = 8.1 Hz, 2H, Ar–H), 7.85 (d, *J* = 8.1 Hz, 2H, Ar–H), 8.16 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 93.10, 113.21, 117.69, 118.36, 133.82, 137.30, 147.67, 151.46, 153.55, 165.16 ppm; MS (EI): *m*/*z* = 253 (M^+), 228, 161.

2-(Cyanoamino)-4-hydroxy-6-(4-methoxyphenyl)-pyrimidine-5-carbonitrile (**7c**, $C_{13}H_9N_5O_2$)
White solid; m.p.: 122–124 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,339, 3,210, 2,825, 2,243, 1,668, 1,583, 1,562, 1,421, 804 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 371, 261 nm; ^{1}H NMR ($CDCl_3$): δ = 2.82 (bs, 1H, NH), 3.87 (s, 3H, CH_3), 7.14–8.01 (m, 4H, Ar–H), 8.10 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 53.26, 96.18, 113.14, 116.57, 117.64, 130.76, 135.30, 150.04, 153.67, 146.71, 163.55 ppm; MS (EI): *m*/*z* = 267 (M^+), 237, 161.

2-(Cyanoamino)-4-(4-(dimethylamino)phenyl)-6-hydroxypyrimidine-5-carbonitrile (**7d**, $C_{14}H_{12}N_6O$)
Red solid; m.p.: 140–142 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,341, 3,247, 2,827, 2,251, 1,670, 1,572, 1,558, 1,449, 813 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 368, 268 nm; ^{1}H NMR ($CDCl_3$): δ = 3.07 (s, 6H, CH_3), 3.78 (bs, 1H, NH), 6.82 (d, *J* = 7.9 Hz, 2H, Ar–H), 7.95 (d, *J* = 7.9 Hz, 2H, Ar–H), 8.10 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 52.62, 91.69, 111.70, 117.51, 118.27, 133.81, 153.77, 154.26, 163.98 ppm; MS (EI): *m*/*z* = 280 (M^+), 237, 161.

2-(Cyanoamino)-4-hydroxy-6-(4-methylphenyl)pyrimidine-5-carbonitrile (**7e**, $C_{13}H_9N_5O$)
White solid; m.p.: 89–102 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,336, 3,232, 2,810, 2,262, 1,690, 1,562, 1,551, 1,440, 823 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 354, 262 nm; ^{1}H NMR ($CDCl_3$): δ = 2.57 (s, 3H, CH_3), 3.61 (bs, 1H, NH), 6.80 (d, *J* = 8.1 Hz, 2H, Ar–H), 7.21 (d, *J* = 8.1 Hz, 2H, Ar–H), 8.26 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 28.67, 90.55, 112.10, 116.48, 117.49, 132.80, 151.73, 154.44, 165.67 ppm; MS (EI): *m*/*z* = 251 (M^+), 237, 161.

2-(Cyanoamino)-4-hydroxy-6-(4-nitrophenyl)pyrimidine-5-carbonitrile (**7f**, $C_{12}H_6N_6O_3$)
Orange solid; m.p.: 130–132 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,382, 3,210, 2,843, 2,223, 1,681, 1,556, 1,429, 838 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 371, 261 nm; ^{1}H NMR ($CDCl_3$): δ = 6.13 (bs, 1H, NH), 7.23–8.21 (m, 4H, Ar–H), 8.71 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 99.87, 113.15, 116.44, 118.24, 133.46, 134. 25, 152.13, 153.56, 166.51 ppm; MS (EI): *m*/*z* = 282 (M^+), 237, 161.

2-(Cyanoamino)-6-(3,5-dimethoxyphenyl)-4-hydroxy-pyrimidine-5-carbonitrile (**7g**, $C_{14}H_{11}N_5O_3$)
Yellow solid; m.p.: 118–120 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,341, = 3,341, 3,320, 2,841, 2,227, 1,640, 1,565, 1,451, 1,440, 815 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 356, 251 nm; ^{1}H NMR ($CDCl_3$): δ = 3.76 (s, 3H, CH_3), 3.79 (s, 3H, CH_3), 3.91 (bs, 1H, NH), 6.23 (s, 1H, Ar–H), 8.35 (s, 2H, Ar–H), 8.20 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 53.10, 54.22, 95.51, 113.21, 116.61, 128.55, 132.91, 134.81, 147.20, 152.19, 155.65, 166.19 ppm; MS (EI): *m*/*z* = 397 (M^+), 267, 237.

2-(Cyanoamino)-4-hydroxy-6-(4-pyridyl)-pyrimidine-5-carbonitrile (**7h**, $C_{11}H_6N_6O$)
Yellow solid; m.p.: 190–192 °C (EtOH); IR (KBr): $\bar{\nu}$ = 3,351, 3,326, 2,821, 2,219, 1,652, 1,580, 1,456, 1,441, 805 cm^{-1}; UV–vis (95% EtOH): λ_{max} = 352, 257 nm; ^{1}H NMR ($CDCl_3$): δ = 3.81 (bs, 1H, NH), 7.40 (d, *J* = 8.0 Hz, 2H, Py-H), 8.15 (d, *J* = 8.0 Hz, 2H, Py-H), 9.63 (s, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$): δ = 93.66, 113.56, 117.41, 123.51, 133.20, 135.41, 153.66, 155.60, 166.53 ppm; MS (EI): *m*/*z* = 238 (M^+), 161.

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