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An efficient and convenient one-pot multicomponent synthesis of novel pyrimidine derivatives: *N*-(4-aryl-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamides

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Abstracts An efficient and facile synthesis of novel pyrimidine derivatives, *N*-(4-aryl-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamides, via one-pot multicomponent reaction of different aromatic aldehydes, 2-acetylpyridine, and cyanoguanidine in the presence of NaOH in anhydrous EtOH is reported. Pyrimidine derivatives are extremely important six membered aromatic heterocyclic rings containing two nitrogen atoms which have a wide variety of important biologically activity. This method has the advantages of easy work-up, convenient purification, short reaction times, and high yields.

Keywords Multicomponent reaction · *N*-((Pyridin-2-yl)pyrimidin-2-yl)cyanamide · 2-Acetylpyridine · Cyanoguanidine · Synthesis

Introduction

Multicomponent reactions (MCRs) have emerged as efficient and powerful tools in modern synthetic organic chemistry, because the synthesis of complex organic molecules from simple and readily available substrates can be achieved in a very fast and efficient manner without the isolation of any intermediates [1–6]. Therefore, developing new MCRs and improving known MCRs are popular areas of research in current organic synthesis. Pyrimidine and its derivatives, for example purines, pyrrolopyrimidines, pyrazolopyrimidines, etc., form parts the structures of

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many biologically active compounds and have many medical and biological properties [7–10]. For example, 4*H*-pyrido[1,2-*a*]pyrimidin-4-ones have been used as anticancer agents and HIV-integrase inhibitors [11, 12], and pteridines are potent antitumor agents [13]. Although many kinds of pyrimidine derivative have been prepared by use of different synthetic methods [14–18], it is still very essential to find novel methods to prepare more new pyrimidine derivatives. In continuation of our ongoing endeavors using MCRs for synthesis of organic compounds [19–21], herein we report a practical and simple method of preparation of pyrimidine derivatives by reaction of aromatic aldehydes, 2-acetylpyridine, and cyanoguanidine under mild conditions.

Results and discussion

We have synthesized pyridylpyrimidine-2-amine in the presence of NaOH under solvent-free conditions [22]. On the basis of this synthesis, we tried to prepare new pyrimidines by three-component reaction of aldehyde, 2-acetylpyridines, and cyanoguanidine in the presence of NaOH under solvent-free conditions. However, we did not obtain the desired products.

We then investigated three-component reaction of 4-fluorobenzaldehyde **1a** (1 mmol), 2-acetylpyridines **2** (1 mmol), and cyanoguanidine **3** (1.5 mmol) as model reaction with different solvents and different catalysts.

First, several alkaline and acidic catalysts were examined to set up the standard reaction conditions. The experimental results showed that the acidic catalysts have no effect of this reaction. However, we found the reaction could proceed promisingly under basic conditions. A variety of basic catalysts, for example NaOH, KOH, Na_2CO_3, K_2CO_3, Et_3N, and DBU, were then examined in this model reaction. We found weak inorganic bases, for example Na_2CO_3 and K_2CO_3, and organic bases, for example Et_3N and DBU, were not the efficient catalysts of this synthesis. Strong inorganic bases, for example NaOH and KOH were sufficiently active to promote this reaction.

Second, because solvents are generally important in multi-component reactions, we also investigated the effect of solvent in this reaction. A variety of solvents, for example anhydrous ethanol, methanol, DMF, acetonitrile, tetrahydrofuran, and toluene, were tested in the model reaction under their respective reflux conditions (DMF 80 °C). We found that this reaction proceeded smoothly in protonic solvents, for example ethanol and methanol, but that non-protonic solvents, for example acetonitrile and toluene, were unsuitable for this synthesis. The optimized results are listed in Table 1. Taking into account the cost, toxicity, reaction time, and catalytic properties of the catalysts and solvents, we chose NaOH and EtOH as the preferred catalyst and solvent to conduct these syntheses.

Finally, we studied the model reaction at different temperatures. The reaction was conducted at room temperature, 40, 50, 60, 70, 80, and 90 °C. The appropriate temperature for this reaction was 80 °C; yields were not significantly improved by use of higher temperatures (Table 2).

Table 1 Synthesis of **4a** in the presence of different catalysts and solvents

Entry	Catalyst	Solvent	Time (h)	Yield[a] (%)
1	Et_3N	EtOH	2	8
2	$C_5H_{11}N$	EtOH	2	5
3	DBU	EtOH	2	0
4	$MgCl_2$	EtOH	2	0
5	$FeCl_3$	EtOH	2	0
6	$ZnCl_2$	EtOH	2	0
7	$SnCl_2$	EtOH	2	0
8	Na_2CO_3	EtOH	2	25
9	K_2CO_3	EtOH	2	28
10	Cs_2CO_3	EtOH	2	21
11	KOH	EtOH	2	87
12	KOH	None	2	0
13	NaOH	None	2	0
14	**NaOH**	**EtOH**	**1**	**93**
15	NaOH	DMF[b]	1	20
16	NaOH	THF	1	12
17	NaOH	MeOH	1	90
18	NaOH	Toluene	1	0
19	NaOH	CH_3CN	1	0
20	NaOH	EtOH	1.5	93
21	NaOH	EtOH	2	94
22	NaOH	EtOH	3	94

Reagents and conditions: 4-fluorobenzaldehyde **1a** (1 mmol), 2-acetylpyridine **2** (1 mmol), guanidine carbonate **3** (1.5 mmol), and NaOH (2 mmol), solvent (10 mL), reflux, anhydrous EtOH; bold indicates the chosen catalyst and solvent

[a] Isolated yields

[b] Reaction temperature 80 °C

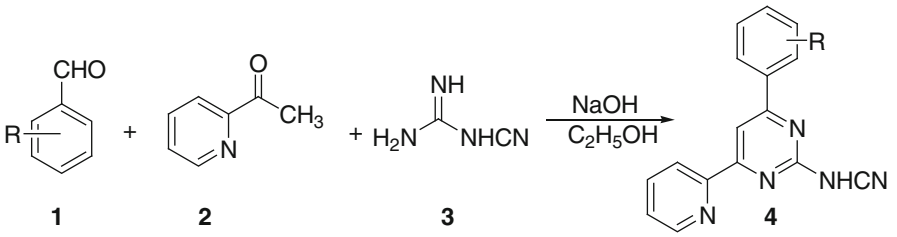
Table 2 Synthesis of **4a** at different temperatures

Entry	Catalyst	Temp. (°C)	Yield[a] (%)
1	NaOH	r.t.	20
2	NaOH	40	25
3	NaOH	50	45
4	NaOH	60	50
5	NaOH	70	65
6	**NaOH**	**80**	**93**
7	NaOH	90	94

Bold indicates the best temperature conditions

Under these optimized reaction conditions, a variety of aromatic aldehydes were reacted with 2-acetylpyridine and cyanoguanidine in this three-component reaction (Scheme 1). The results obtained are listed in Table 3. As shown in Table 3, fifteen compounds were synthesized. Irrespective of whether electron-withdrawing (for example F, Cl, Br) or electron-donating (for example CH_3–, CH_3O–) substituents were present on the aromatic aldehydes, the products were obtained in high yield. The properties of the substituent groups had no obvious effect on these reactions.

All the new target compounds were completely characterized by IR, ^{1}H NMR, ^{13}C NMR, and HRMS. For example, the ^{1}H NMR spectrum of **4i** contains a singlet



Scheme 1 Synthesis of *N*-(4-aryl-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamides

Table 3 Results from synthesis of compounds **4**

Entry	*R*	Product	Yields (%)
1	2-F	**4a**	93
2	3-F	**4b**	91
3	4-F	**4c**	90
4	2-Br	**4d**	93
5	4-Br	**4e**	95
6	4-Cl	**4f**	94
7	2,4-Cl_2	**4g**	93
8	3,4-Cl_2	**4h**	92
9	4-CH_3	**4i**	94
10	3,4-$(CH_3)_2$	**4j**	96
11	3-CH_3O	**4k**	93
12	2,5-$(CH_3O)_2$	**4l**	91
13	3,4-$(CH_3O)_2$	**4m**	91
14	3,4,5-$(CH_3O)_3$	**4n**	94
15	3,4-OCH_2O	**4o**	93

at delta 2.37 from the CH_3 protons and a singlet at delta 11.64 from the NHCN protons. The spectrum also contains doublets at delta 7.35 ppm ($J = 7.6$ Hz), 8.35 ppm ($J = 7.5$ Hz), and 8.78 ppm ($J = 6.9$ Hz), a multiplet at delta 8.01–8.09 ppm, and a triplet at delta 7.59 ppm ($J = 5.1$ Hz) from the nine aryl protons. In ^{13}C NMR, the chemical shifts of the 17 carbon atoms were at 20.98, 106.14, 110.53, 121.38, 127.02, 129.59, 132.56, 137.60, 141.69, 149.64, 152.40, 158.86, 164.42, and 165.72. In the HRMS spectrum, the calculated *m/z* for $C_{17}H_{13}N_5$ $[M + Na]^+$ is 310.1069, and we found *m/z* is 310.1046.

Conclusions

An efficient one-pot multi-component reaction has been developed for synthesis of *N*-(4-aryl-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamides from simple and readily available starting materials in the presence of NaOH in ethanol. The products are novel tridentate ligands that can be used to construct important metal–organic complexes

(coordination compounds). The method has many advantages, for example mild conditions, inexpensive reagents, easily obtained catalyst, short reaction time, and high yields.

Experimental

Melting points were determined on XT-5 melting-point apparatus with microscope and are uncorrected. IR spectra were recorded on a FT Bruker Tensor 27 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were obtained from solution in $CDCl_3$, with Me_4Si as internal standard, using a Bruker-300 spectrometer. HRMS spectra were obtained with a Bruker microTOF-Q 134 instrument.

General procedure for synthesis of *N*-(4-aryl-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide derivatives

The mixture of aromatic aldehyde **1** (1 mmol), 2-acetylpyridine **2** (1 mmol), cyano guanidine **3** (1.5 mmol), and NaOH (2 mmol) was placed in a reaction flask with anhydrous EtOH and heated at <80 °C for approximately 1 h. After completion of the reaction, the mixture was poured into water (0.5 % HCl), and then washed thoroughly with water. The product was isolated by filtration, dried, and recrystallized from 95 % ethanol.

*N-(4-(2-Fluorophenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4a**)*

m.p. 211–212 °C; IR (KBr) *v*: 3,370, 2,925, 2,361, 2,341, 2,187, 1,683, 1,610, 1,523, 1,489, 1,458, 1,430, 1,312, 1,220, 1,102, 1,023, 993, 770, 711, 670 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.37–7.45 (3H, m, ArH), 7.59–7.65 (2H, m, ArH), 8.03–8.14 (2H, m, ArH), 8.41 (1H, d, $J = 1.8$ Hz, ArH), 8.79 (1H, d, $J = 4.2$ Hz, ArH), 11.80 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 110.47, 116.71, 119.58, 121.45, 125.08, 130.58, 133.36, 137.56, 149.79, 152.20, 155.46, 158.93, 162.36, 164.69, 164.75.

HRMS *m/z* calculated for $C_{16}H_{10}FN_5$ $[M + Na]^+$: 314.0818, found: 314.0810.

*N-(4-(3-Fluorophenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4b**)*

m.p. 198–199 °C; IR (KBr) *v*: 3,365, 2,932, 2,360, 2,341, 1,716, 1,651, 1,541, 1,488, 1,353, 1,242, 774, 669 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.43 (1H, t, $J = 6.3$ Hz, ArH), 7.61–7.66 (2H, m, ArH), 7.99 (1H, d, $J = 8.1$ Hz, ArH), 8.06–8.09 (2H, m, ArH), 8.37 (1H, d, $J = 5.7$ Hz, ArH), 8.47 (1H, s, ArH), 8.79 (1H, d, $J = 3.3$ Hz, ArH), 11.77 (1H, s, NHCN). ^{13}C NMR (400 MHz, DMSO) δ: 110.35, 106.87, 110.00, 112.72, 113.54, 118.08, 121.41, 125.94, 130.79, 137.53, 149.39, 152.27, 158.73, 161.28, 164.36.

HRMS *m/z* calculated for $C_{16}H_{10}FN_5$ $[M + H]^+$: 292.0998, found: 292.0994.

*N-(4-(4-Fluorophenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4c**)*

m.p. 160–161 °C; IR (KBr) *v*: 3,350, 2,839, 2,360, 2,341, 2,251, 1,716, 1,651, 1,604, 1,540, 1,507, 1,487, 1,411, 1,362, 1,235, 1,154, 1,097, 836, 777, 669, 570 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.47 (2H, t, $J = 8.4$ Hz, ArH), 7.62 (1H, s, ArH), 8.06 (1H, t, $J = 6.0$ Hz, ArH), 8.28 (2H, s, ArH), 8.36 (1H, d, $J = 7.8$ Hz, ArH), 8.42 (1H, s, ArH), 8.69 (1H, s, ArH), 11.77 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 106.46, 110.42, 116.04, 121.46, 126.24, 129.74, 131.95, 137.69, 149.69, 152.34, 158.91, 162.55, 164.81, 165.86.

HRMS *m/z* calculated for $C_{16}H_{10}FN_5$ $[M + H]^+$: 292.0998, found: 292.0980.

*N-(4-(2-Bromophenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4d**)*

m.p. 182–183 °C; IR (KBr) *v*: 3,350, 2,980, 2,360, 2,341, 1,748, 1,716, 1,698, 1,651, 1,540, 1,507, 1,473, 1,456, 1,418, 1,340, 773, 669, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.50–7.56 (1H, m, ArH), 7.59–7.63 (1H, m, ArH), 7.78 (1H, d, $J = 7.8$ Hz, ArH), 8.05 (1H, t, $J = 7.5$ Hz, ArH), 8.18 (1H, d, $J = 6.9$ Hz, ArH), 8.35 (2H, d, $J = 7.8$ Hz, ArH), 8.43 (1H, d, $J = 8.7$ Hz, ArH), 8.78 (1H, d, $J = 3.3$ Hz, ArH), 11.76 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 106.96, 110.27, 121.50, 126.16, 126.24, 126.29, 129.55, 131.18, 134.14, 137.70, 149.68, 152.22, 158.90, 164.24, 164.97.

HRMS *m/z* calculated for $C_{16}H_{10}BrN_5$ $[M + H]^+$: 352.0198, found: 352.0188.

*N-(4-(4-Bromophenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4e**)*

m.p. 181–182 °C; IR (KBr) *v*: 3,365, 2,988, 2,360, 2,341, 2,249, 1,716, 1,698, 1,647, 1,540, 1,474, 1,421, 1,399, 1,360, 1,072, 1,008, 830, 794, 777, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.64 (1H, t, $J = 6.0$ Hz, ArH), 7.81 (2H, d, $J = 8.4$ Hz, ArH), 8.06–8.12 (1H, m, ArH), 8.19 (2H, d, $J = 8.7$ Hz, ArH), 8.39 (1H, d, $J = 7.8$ Hz, ArH), 8.49 (1H, s, ArH), 8.81 (1H, d, $J = 3.9$ Hz, ArH), 11.79 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 103.20, 106.70, 118.30, 121.52, 125.09, 129.16, 132.11, 137.79, 144.38, 149.77, 151.50, 152.31, 155.30, 164.80.

HRMS *m/z* calculated for $C_{16}H_{10}BrN_5$ $[M + H]^+$: 352.0198, found: 352.0163.

*N-(4-(4-Chlorophenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4f**)*

m.p. 180–181 °C; IR (KBr) *v*: 3,351, 2,955, 2,360, 2,341, 1,716, 1,652, 1,541, 1,362, 832, 791, 778, 669 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.62–7.67 (3H, m, ArH), 8.05–8.11 (1H, m, ArH), 8.23–8.27 (2H, m, ArH), 8.39 (1H, d, $J = 8.1$ Hz, ArH), 8.47 (1H, d, $J = 3.9$ Hz, ArH), 8.80 (1H, d, $J = 3.6$ Hz, ArH), 11.79 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 102, 26, 110.30, 121.51, 126.35, 128.89, 129.16, 134.14, 136.45, 137.78, 141.60, 149.75, 152.28, 158.92, 165.20, 166.73.

HRMS *m/z* calculated for $C_{16}H_{10}ClN_5$ $[M + H]^+$: 308.0703, found: 308.0685.

*N-(4-(2,4-Dichlorophenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4g**)*

m.p. 205–206 °C; IR (KBr) *v*: 3,360, 2,840, 2,360, 2,341, 2,239, 1,716, 1,652, 1,590, 1,557, 1,539, 1,474, 1,419, 1,375, 1,354, 1,231, 1,105, 1,052, 1,002, 868, 843, 819, 781, 747, 721, 669, 574 cm^{-1}; ^1H NMR (300 MH, $CDCl_3$) δ: 7.61–7.67 (2H, m, ArH), 7.77 (1H, d, $J = 8.4$ Hz, ArH), 7.85 (1H, d, $J = 3.6$ Hz, ArH), 8.07–8.12 (1H, m, ArH), 8.27 (1H, s, ArH), 8.41 (1H, d, $J = 7.8$ Hz, ArH), 8.79 (1H, d, $J = 4.2$ Hz, ArH), 11.94 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 102.26, 105.14, 107.44, 109.73, 110.89, 111.62, 112.40, 121.58, 127.94, 132.65, 137.87, 143.84, 149.88, 152.04, 154.09, 165.03.

HRMS *m/z* calculated for $C_{16}H_9Cl_2N_5$ $[M + Na]^+$: 364.0133, found: 364.0114.

*N-(4-(3,4-Dichlorophenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4h**)*

m.p. 180–181 °C; IR (KBr) *v*: 3,370, 2,985, 2,360, 2,341, 2,250, 1,748, 1,716, 1,698, 1,647, 1,540, 1,488, 1,424, 1,361, 1,092, 832, 777, 669 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.60–7.65 (2H, m, ArH), 8.02–8.09 (1H, m, ArH), 8.23 (2H, d, $J = 8.7$ Hz ArH), 8.37 (1H, d, $J = 8.4$ Hz, ArH), 8.43 (1H, s, ArH), 8.78 (1H, d, $J = 3.9$ Hz, ArH), 11.74 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 106.61, 110.35, 121.47, 126.28, 128.90, 129.00, 134.24, 136.42, 137.70, 149.70, 152.28, 158.96, 164.65, 164.87, 164.89.

HRMS *m/z* calculated for $C_{16}H_9Cl_2N_5$ $[M + Na]^+$: 364.0133, found: 364.0168.

*N-(4-(Pyridin-2-yl)-6-p-tolylpyrimidin-2-yl)cyanamide (**4i**)*

m.p. 168–169 °C; IR (KBr) *v*: 3,370, 3,153, 2,361, 2,341, 2,233, 1,699, 1,684, 1,653, 1,597, 1,578, 1,539, 1,507, 1,458, 1,457, 1,420, 1,347, 1,232, 825, 800, 778, 721, 669 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.37 (3H, s, CH_3), 7.35 (2H, d, $J = 7.8$ Hz, ArH), 7.59 (1H, t, $J = 5.1$ Hz, ArH), 8.01–8.09 (3H, m, ArH), 8.35 (2H, d, $J = 7.5$ Hz, ArH), 8.78 (1H, d, $J = 6.9$ Hz, ArH), 11.64 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 20.98, 106.14, 110.35, 121.38, 126.13, 127.02, 129.59, 129.69, 132.56, 137.60, 141.69, 149.64, 149.70, 152.40, 158.86, 164.42, 165.72.

HRMS *m/z* calculated for $C_{17}H_{13}N_5$ $[M + Na]^+$: 310.1069, found: 310.1046.

*N-(4-(3,4-Dimethylphenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4j**)*

m.p. 122–123 °C; IR (KBr) *v*: 3,366, 2,980, 2,360, 2,341, 2,227, 1,646, 1,575, 1,557, 1,539, 1,506, 1,472, 1,456, 1,418, 1,351, 1,090, 994, 775, 668 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.29 (3H, s, CH_3), 2.31 (3H, s, CH_3), 7.31 (1H, d, $J = 8.1$ Hz, ArH), 7.62–7.34 (1H, q, $J = 7.8$ Hz, ArH), 7.92 (1H, d, $J = 7.8$ Hz, ArH), 7.96 (1H, s, ArH), 8.03–8.09 (1H, m, ArH), 8.36 (1H, s, ArH), 8.38 (1H, s, ArH), 8.79 (1H, d, $J = 4.2$ Hz, ArH), 11.70 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 19.39, 102.27, 106.12, 110.63, 121.41, 124.63, 126.16, 127.91, 130.12, 132.91, 137.04, 137.65, 140.52, 140.55, 149.66, 152.47, 158.92, 165.91.

HRMS *m/z* calculated for $C_{18}H_{15}N_5$ $[M + Na]^+$: 324.1225, found: 324.1204.

*N-(4-(3-Methoxyphenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4k**)*

m.p. 164–165 °C; IR (KBr) *v*: 3,343, 2,980, 2,361, 2,250, 1,717, 1,698, 1,648, 1,541, 1,508, 1,488, 1,457, 1,420, 1,352, 1,285, 1,262, 1,247, 1,045, 796, 770, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 3.84 (3H, s CH_3O), 7.14 (1H, dd, $J = 2.1$ Hz, $J = 8.1$ Hz, ArH), 7.46 (1H, t, $J = 8.1$ Hz, ArH), 7.59 (1H, dd, $J = 2.1$ Hz, $J = 6.9$ Hz, ArH), 7.68 (1H, s, ArH), 7.74 (1H, d, $J = 7.8$ Hz, ArH), 8.03 (1H, t, $J = 7.8$ Hz, ArH), 8.36 (2H, d, $J = 10.2$ Hz, ArH), 8.77 (1H, d $J = 7.5$ Hz, ArH), 11.66 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 55.22, 106.78, 110.41, 112.11, 112.16, 117.21, 119.45, 121.44, 126.15, 130.11, 136.82, 137.58, 149.64, 149.70, 152.35, 158.80, 159.63, 164.65, 165.56.

HRMS *m/z* calculated for $C_{17}H_{13}N_5O$ $[M + Na]^+$: 326.1018, found: 326.0968.

*N-(4-(2,5-Dimethoxyphenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4l**)*

m.p. 185–186 °C; IR (KBr) *v*: 3,316, 3,145, 2,999, 2,360, 2,341, 2,181, 1,683, 1,642, 1,594, 1,522, 1,497, 1,466, 1,432, 1,396, 1,311, 1,282, 1,246, 1,220, 1,194, 1,159, 1,101, 1,016, 802, 770, 723, 711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 3.70 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 6.76 (1H, d, $J = 3.0$ Hz, ArH), 6.89 (1H, dd, $J = 3.0$ Hz, $J = 8.7$ Hz, ArH), 7.02 (1H, d, $J = 9.0$ Hz, ArH), 7.41–7.45 (1H, m, ArH), 7.89 (2H, dt, $J = 1.2$ Hz, $J = 5.7$ Hz, ArH), 8.63 (1H, d, $J = 3.3$ Hz, ArH), 8.95 (1H, s, ArH), 11.70 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 55.40, 55.16, 101.64, 112.51, 112.71, 113.38, 116.97, 119.47, 124.01, 130.45, 131.00, 137.39, 137.41, 147.98, 148.44, 149.95, 153.34, 155.92.

HRMS *m/z* calculated for $C_{18}H_{15}N_5O_2$ $[M + Na]^+$: 356.1123, found: 356.1142.

*N-(4-(3,4-Dimethoxyphenyl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4m**)*

m.p. 193–194 °C; IR (KBr) *v*: 3,296, 2,360, 2,341, 2,235, 2,181, 1,599, 1,577, 1,539, 1,519, 1,506, 1,419, 1,376, 1,353, 1,318, 1,263, 1,214, 1,174, 1,132, 1,019, 871, 818, 779, 765, 669, 600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 3.94 (3H, s, OCH_3), 3.97 (3H, s, OCH_3), 6.93 (1H, d, $J = 6.3$ Hz, ArH), 7.45–7.48 (1H, m, ArH), 7.78 (2H, d, $J = 6.0$ Hz, ArH), 7.87–7.91 (1H, m, ArH), 8.20 (1H, s, ArH), 8.37 (1H, d, $J = 5.7$ Hz, ArH), 8.79 (1H, d, $J = 3.3$ Hz, ArH). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 55.50, 55.97, 109.90, 110.80, 115.40, 119.44, 121.23, 122.18, 125.88, 127.92, 137.40, 149.18, 149.50, 152.33, 158.43, 165.61.

HRMS *m/z* calculated for $C_{18}H_{15}N_5O_2$ $[M + Na]^+$: 356.1123, found: 356.1105.

*N-(4-(Pyridin-2-yl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl)cyanamide (**4n**)*

m.p. 229–230 °C; IR (KBr) *v*: 3,330, 2,942, 2,360, 2,340, 1,601, 1,581, 1,540, 1,470, 1,455, 1,424, 1,373, 1,345, 1,248, 1,220, 1,126, 985, 855, 797, 777, 741, 697, 658 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 3.96 (3H, s OCH_3), 4.01 (6H, s $2 \times OCH_3$), 7.48–7.51 (3H, m, ArH), 7.93 (1H, t, $J = 5.7$ Hz, ArH), 8.42 (1H, s, ArH), 8.50 (1H, d, $J = 5.2$ Hz, ArH), 8.78–8.80 (1H, m, ArH). ^{13}C NMR

(300 MHz, $CDCl_3$) δ: 56.50, 60.59, 104.99, 105.02, 122.03, 126.63, 133.11, 138.11, 140.97, 150.12, 153.60, 159.17, 165.02.

HRMS *m/z* calculated for $C_{19}H_{17}N_5O_3$ $[M + Na]^+$: 386.1229, found: 386.1228.

*N-(4-(Benzo[d][1,3]dioxol-5-yl)-6-(pyridin-2-yl)pyrimidin-2-yl)cyanamide (**4o**)*

m.p. 225–226 °C; IR (KBr) *v*: 3,335, 2,909, 2,360, 2,341, 1,601, 1,585, 1,537, 1,504, 1,488, 1,445, 1,426, 1,384, 1,364, 1,332, 1,267, 1,243, 1,213, 1,110, 1,093, 1,040, 932, 852, 824, 789, 775, 671 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 6.16 (2H, s, OCH_2O), 7.10 (1H, d, $J = 8.4$ Hz, ArH), 7.60 (1H, dd, $J = 5.1$ Hz, $J = 6.6$ Hz, ArH), 7.72 (1H, s, ArH), 7.82 (1H, d, $J = 8.1$ Hz, ArH), 8.06 (1H, t, $J = 7.8$ Hz, ArH), 8.35 (2H, d, $J = 8.4$ Hz, ArH), 8.79 (1H, d, $J = 4.5$ Hz, ArH), 11.62 (1H, s, NHCN). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 101.89, 106.71, 108.64, 121.90, 122.41, 126.13, 129.46, 137.64, 137.68, 137.71, 148.06, 148.12, 149.65, 150.33, 158.68, 165.22.

HRMS *m/z* calculated for $C_{17}H_{11}N_5O_2$ $[M + H]^+$: 318.0991, found: 318.0978.

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