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ORIGINAL ARTICLE

A green one-pot three-component cascade reaction: the synthesis of 2-amino-5,8-dihydro-3H-pyrido[2,3-D]pyrimidin-4-ones in aqueous medium

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Abstract A one-pot three-component cascade reaction for the green synthesis of a new class of 2-amino-5,8-dihydro-3H-pyrido[2,3-d]pyrimidin-4-ones was developed from the condensation of aromatic aldehydes with 2,6-diamino pyrimidin-4(3H)-one and acetophenone derivatives or various cyclic ketones in the presence of a catalytic amount of sodium carbonate in a mixture of water and ethanol at 60 °C. This reaction led to the construction of two carbon–carbon bonds and one carbon–nitrogen bond in a single synthetic step.

Keywords Green synthesis · Three-component reaction · Dihydropyridopyrimidine · Acetophenone · 2, 6-Diaminopyrimidin-4(3H)-one · MCR

Introduction

The pyrido[2,3-d]pyrimidine scaffold is present in a number of compounds showing a variety of biological properties, such as anticancer [1,2], antitumor [3], antimicrobial [4] and antibacterial activities [5,6]. Pterin and folic acid, a natural pigment and an essential vitamin, respectively, have a pyrazino[2,3-d]pyrimidine core. Folic acid (**I**) has a role in many prominent biological processes including DNA synthesis, DNA repair and cell division [7]. Additionally, several derivatives having this scaffold (e.g., **II**) were found to induce inhibition of cyclin-dependent kinase and induce apoptosis and/or reduce cell proliferation in different solid tumors and leukemia cell lines [8] (Fig. 1).

The most direct synthetic routes to pyrido[2,3-d] pyrimidines are via condensation of heterocyclic amines such as 2,6-diaminopyrimidin-4(3H)-one (**1**) and 6-amino-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one and aldehydes (or isatin) with various cyclic and acyclic ketones under a variety of reaction conditions. Some other methods are reported based on two-component reaction of 2,6-diaminopyrimidin-4(3H)-ones and chained conjugated aldehydes or ketones [9–17]. However, most of the methods have one or more limitations that may include moderate yields, harsh reaction conditions, long reaction times and use of nongreen organic solvents or catalysts [18–23]. Furthermore, all of these methods are reported for ketones containing an active α-hydrogen such as various β-dicarbonyl compounds and diphenylethanones in the presence of metal catalysts under microwave irradiation which give products only in moderate yields [24–29].

The use of toxic and hazardous solvents and catalysts in organic synthesis is considered a huge problem for health, safety of workers and environmental pollution. Green chemistry aims to eliminate the use of toxic solvents and catalysts and replace them with greener alternatives by re-engineering the selection approach of new substrates, innovative changes of the catalyst, greener solvents or using of solvent- and catalyst-free conditions [30,31].

In continuation of our interest in using multi-component reactions (MCRs) in organic synthesis [32–35], herein we describe a complementary approach toward the synthesis of new 2-amino-5,8-dihydro-3H-pyrido[2,3-d]pyrimidin-4-ones via a new three-component condensation reaction using an aromatic aldehyde, 2,6-diaminopyrimidin-4(3H)-one and acetophenone derivatives or cyclic ketones in the presence of

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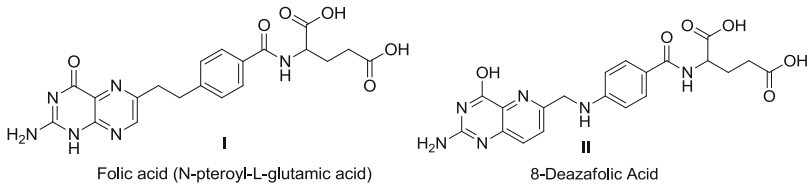
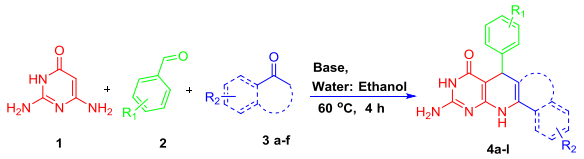
Fig. 1 Biologically active fused pyrimidine derivatives





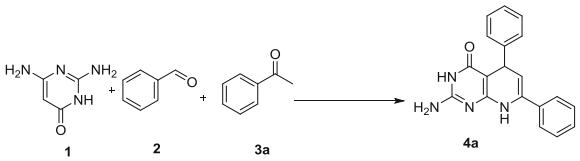
Scheme 1 Synthesis of 2-amino-5,8-dihydro-3H-pyrido[2,3-d]pyrimidin-4-one derivatives (4a-l)

a catalytic amount of an inorganic base in aqueous medium at low temperature and short reaction times. This process is a straightforward approach for the synthesis of fused dihydropyridine and pyrimidine rings due to the suitable change in selection of substrates which simplified the reaction procedure and includes the use of a green solvent and a catalyst (Scheme 1).

Results and discussion

In order to investigate the optimal reaction conditions, we chose the reaction of benzaldehyde, acetophenone and 2,6-diaminopyrimidin-4(3H)-one as a model system. At first, the reaction rate was compared in different solvents using isolated yields of products with identical amounts of reactants where different catalysts are used with respect to the nature of the solvent (i.e., Na_2CO_3 in protic and Et_3N in aprotic) at 60 °C (entries 1–9). The expected product **4a** was scarcely obtained in nonpolar and aprotic polar solvents. Additionally, the reaction failed in the absence of catalyst in ethanol. It was found that the addition of water to the ethanol solution in the presence of Na_2CO_3 can improve the reaction yield significantly (entries 10–12). As seen in entry 12, **4a** was qualitatively obtained in water/ethanol (1:3). Next, the model reaction was studied in water/ethanol at various temperatures. As indicated in Table 1, when the temperature raised the reaction rate increased (entries 13–15). At 60 °C, the maximum yield (98%) was obtained after 4 h. The model reaction was examined in water/ethanol (1:3) at 60 °C using different bases (entries 16–20). The best results were obtained using 10 mol % of Na_2CO_3 or K_2CO_3, and Na_2CO_3 was chosen since it is more affordable than K_2CO_3. As seen in Table 1, it

Table 1 Optimization of the reaction conditions



Entry	Solvent	T (°C)	Catalyst (mol%)	Time (h)	Yield[a] (%)
1	Water	60	Na_2CO_3 (10)	5	60
2	Ethanol	60	Na_2CO_3 (10)	4	80
3	Ethanol	60	–	24	Trace
4	Methanol	60	Na_2CO_3 (10)	12	58
5	Ethyl acetate	60	Et_3N (20)	12	Trace
6	Acetonitrile	60	Et_3N (20)	24	Trace
7	Toluene	110	Et_3N (20)	24	30
8	Dichloromethane	25	Et_3N (20)	24	Trace
9	Water/ethanol (1:1)	60	Na_2CO_3 (10)	4	83
10	Water/ethanol (2:1)	60	Na_2CO_3 (10)	4	70
11	Water/ethanol (1:2)	60	Na_2CO_3 (10)	4	85
12	Water/ethanol (1:3)	60	Na_2CO_3 (10)	4	98
13	Water/ethanol (1:3)	40	Na_2CO_3 (10)	12	62
14	Water/ethanol (1:3)	25	Na_2CO_3 (10)	12	51
15	Water/ethanol (1:3)	60	K_2CO_3 (10)	4	97
16	Water/ethanol (1:3)	60	Et_3N (20)	12	48
17	Water/ethanol (1:3)	60	NaOH (10)	4	93
18	Water/ethanol (1:3)	60	NaOAc (20)	12	70
19	Water/ethanol (1:3)	60	Cs_2CO_3 (20)	6	90

Reaction conditions: 2,6-diaminopyrimidin-4(3H)-one 1 (1 mmol), benzaldehyde 2 (1 mmol), acetophenone 3 (1 mmol)

[a] Isolated yield

Table 2 Synthesis of 2-amino-5,8-dihydro-3H-pyrido[2,3-d]pyrimidin-4-one derivatives

Entry	2	3	Product	Yield[a] (%)	$m.p._{rep}/m.p._{lit}$ (°C)
1	Benzaldehyde	Acetophenone (**3a**)	**4a**	98	>300/>300 [18]
2	4-Chlorobenzaldehyde	Acetophenone (**3a**)	**4b**	95	>300/>300 [18]
3	4-Nitrobenzaldehyde	Acetophenone (**3a**)	**4c**	75	>300
4	4-Methylbenzaldehyde	Acetophenone (**3a**)	**4d**	96	>300/>300 [18]
5	4-Pyridinecarbaldehyde	Acetophenone (**3a**)	**4e**	88	>300
6	2-Naphthaldehyde	Acetophenone (**3a**)	**4f**	90	>300
7	2-Furfuraldehyde	Acetophenone (**3a**)	**4g**	97	>300
8	Benzaldehyde	4-Nitroacetophenone (**3b**)	**4h**	83	295–297/>300 [10]
9	Benzaldehyde	Indanone (**3c**)	**4i**	81	>300
10	Benzaldehyde	Indendione (**3d**)	**4j**	70	>300/>300 [17]
11	Benzaldehyde	Dimedone (**3e**)	**4k**	96	>300/>300 [7]
12	Benzaldehyde	Barbituric acid (**3f**)	**4l**	98	>300

Reaction conditions: 2,6-diaminopyrimidin-4(3H)-one **1** (1 mmol), aldehyde **2** (1 mmol), ketone **3** (1 mmol), Na_2CO_3 (10 mol%), in water/ethanol (1:3) (5 mL), stirred at 60 °C for 4 h
[a]Isolated yield

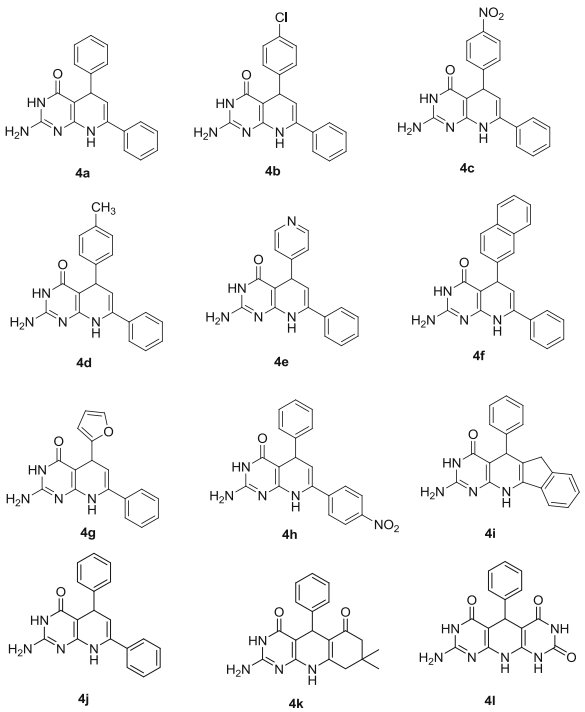
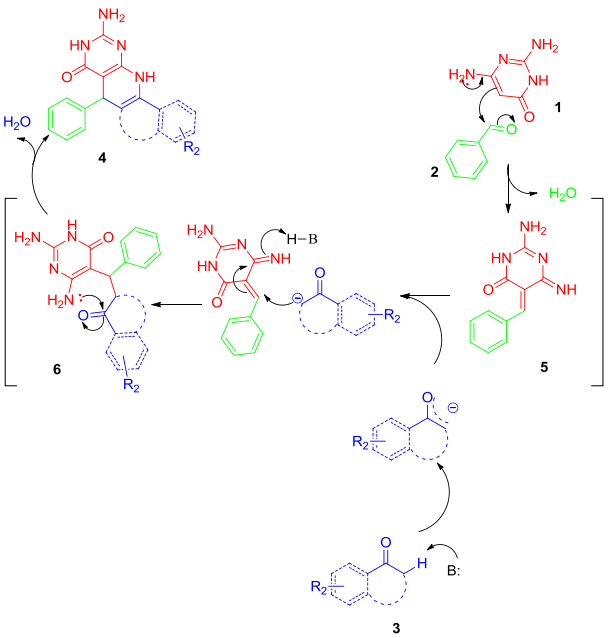


Fig. 2 Structures of products **4a–4l**

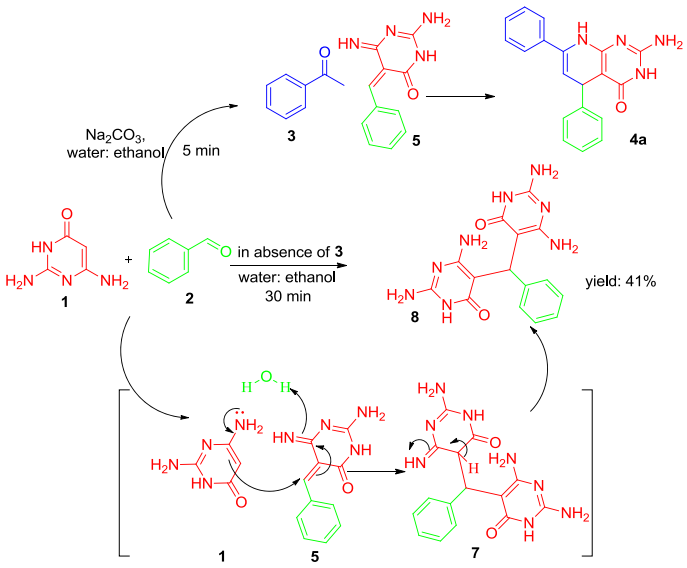


Scheme 2 Proposed reaction mechanism

is clear that the best results were obtained when the reaction was carried out at 60 °C for 4 h in water/ethanol (1:3) using 10 mol % of Na_2CO_3 (entry 12).

With the optimized conditions established above, we next attempted to extend the process to six different ketones (**3a-f**) such as acetophenone, 4-nitroacetophenone, barbituric acid, 1-indanone, indendione and dimedone, and various types of aromatic aldehydes **2** such as benzaldehyde, 4-chlorobenzaldehyde, 4-nitrobenzaldehyde, 4-methylbenzaldehyde, 4-pyridinecarbaldehyde, 2-naphthaldehyde and 2-furfuraldehyde. The results in Table 2 show that all reactions proceeded smoothly to afford the expected 2-amino-5,8-dihydro-3H-pyrido[2,3-d]pyrimidin-4-one derivatives in good to excellent yields, and no undesirable side-reactions were observed under the reported conditions. The obtained products are shown in Fig. 2. All new compounds and some of the known compounds were characterized on the basis of their spectroscopic data (^{1}H and ^{13}C NMR, FTIR, CHN analysis) and by comparison with those reported in the literature.

Scheme 3 Validation of proposed mechanism



A possible mechanism for the formation of products **4a** is shown in Schemes 2, 3. Firstly, a condensation between 2,6-diaminopyrimidin-4(3H)-one **1** and a benzaldehyde **2** would give the imine intermediate **5**. The intermediate **5** undergoes nucleophilic addition of enolate **3** furnishing the intermediate product **6**, which upon intramolecular cyclization and dehydration afforded 2-amino-5,8-dihydro-3H-pyrido[2,3-d]pyrimidin-4-one **4**.

To clarify the proposed mechanism, the imine intermediate **5** was synthesized by reacting 2,6-diaminopyrimidin-4(3H)-one **1** and benzaldehydes **2** in water/ethanol mixture in 5 min in the absence of catalyst (as indicated by TLC). Next, acetophenone **3** and a base were added to the reaction mixture to afford product **4a**. In addition, due to the instability of the intermediate **5**, it was reacted with secondary 2,6-diaminopyrimidin-4(3H)-one **1** producing 5,5′-(phenylmethylene)bis(2,6-diaminopyrimidin-4(3H)-one) **8** in absence of acetophenone after 30 min. These results support the proposed mechanism.

Conclusion

In conclusion, we have developed an environmental and economical three-component approach for the synthesis of a wide range of 2-amino-5,8-dihydro-3H-pyrido[2,3-d]pyrimidin-4-ones from aromatic aldehydes, ketones and 2,6-diaminopyrimidin-4(3H)-one in aqueous medium under mild conditions and short reaction times. This approach provides a high yielding reaction for wide functional group tolerance with very straightforward product isolation. We hope that this approach can be used in the synthesis of bioactive compounds.

Supplementary information

Supplementary data (copies of ^{1}H and ^{13}C NMR spectra for unknown compounds) associated with this article can be found in the online version.

Experimental

All starting materials in this work were purchased from Merck and Fluka Chemical Companies and used without purification. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX-300 Avance spectrometer using DMSO-d_6 as deuterated solvent. Chemical shifts are given in δ relative to tetramethylsilane (TMS) as an internal standard, and coupling constants J are given in Hz. Abbreviations used for ^{1}H NMR signals are s = singlet, d = doublet, m = multiplet and b = broad. Elemental analyses were performed with an Elementar Analysensysteme GmbH VarioEL.

General procedure for synthesis of 2-(1-(alkylcarbamoyl)-2,2-dicyanoethyl)-N-alkylbenzamides *4a-l*

A solution of 2,6-diaminopyrimidin-4(3H)-one (0.13 g, 1 mmol), an aldehyde (1 mmol) and a ketone (1 mmol) in the presence of Na_2CO_3 (0. 01 g, 0.1 mmol) in water/ethanol (1:3) (5 mL) was stirred at 60 °C for 4–6 h. After completion of the reaction, as indicated by TLC with ethyl acetate/*n*-hexane (4:1), the solution was diluted with water. The resulting solid was filtered and washed with water (10 mL).

Then, the solid was crystalized from ethanol to afford pure product.

2-Amino-5,7-diphenyl-5,8 -dihydropyrido[2,3-d]pyrimidin-4(3H) -one *(4a)*

Pale brown solid; mp >300 °C; IR (KBr) ν /cm^{-1} 3400, 3071, 1650, 1609, 1550, 1512; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 4.59 (d, 1H, *J* 3.0, CH), 5.07 (d, 1H, *J* 3.0, CH), 5.77 (OH), 6.20 (s, 2H, NH_2) 7.1–7.5 (m, 10H, H-Ar), 8.36 (s,1H, NH), 10.20 (s, 1H, NH); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 38.1, 88.4, 103.5, 126.0, 127.8, 128.5, 128.6, 128.8, 136.0, 148.8, 154.2, 156.7, 162.3; Anal. Calcd. for $C_{19}H_{16}N_4O$: C, 72.13; H, 5.10; N, 17.71; found C, 72.11; H, 5.15; N, 17.65.

2-(Amino-d_2)-5,7-diphenyl-5,8-dihydropyrido[2,3-d]pyrimidin-4(3H)-one-3,8-d_2 (*4a*, after addition of D_2O)

^{1}H NMR (300.13 MHz, DMSO-d_6 + D_2O) δ 4.63 (d, 1H, *J* 3.0, CH), 5.13 (d, 1H, *J* 3.0, CH), 7.16–7.50 (m, 10H, H–Ar), 8.36 (s,1H, NH), 10.20 (s, 1H, NH).

2-Amino-5-(4 -chlorophenyl)-7- phenyl-5,8-dihydropyrido[2,3-d]pyrimidin-4(3H)-one (*4b*)

Pale brown solid; mp >300 °C; IR (KBr) ν /cm^{-1} 3400, 3071, 1650, 1609, 1550, 1515, 780; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 4.88 (d, 1H, *J* 1.8, CH), 5.34 (d, 1H, *J* 1.8, CH), 5.87 (OH), 6.42 (2H, NH_2), 7.16-7.64 (m, 9H, H–Ar), 8.43 (s,1H, NH), 10.07 (s,1H, NH); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 38.0, 87.8, 103.3, 126.5, 126.7, 127.6, 128.2, 128.9, 136.0, 149.4, 150.1, 152.9, 158.8, 160.0, 163.2; Anal. Calcd. for $C_{19}H_{15}ClN_4O$: C, 65.05; H, 4.31; N, 15.97; found C, 64.98.11; H, 4.28; N, 15.95.

2-Amino-5-(4-nitrophenyl) -7-phenyl-5,8-dihydropyrido[2,3 -d]pyrimidin-4(3H) -one (*4c*)

Yellow solid; mp >300 °C; IR (KBr) ν /cm^{-1} 3400, 3071, 1650, 1609, 1550, 1515, 1350; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 4.77 (d, 1H, *J* 3.0, CH), 5.12 (d, 1H, *J* 3.0, CH), 5.82 (OH), 6.27 (s, 2H, NH_2), 7.35–7.99 (m, 9H, H-Ar), 8.24 (s,1H, NH), 10.24 (s, 1H, NH); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 38.3, 88.8, 103.7, 126.0, 126.3, 127.7, 128.8, 129.0, 136.2, 148.2, 150.8, 154.3, 157.1, 164.8; Anal. Calcd. for $C_{19}H_{15}N_5O_3$: C, 63.15; H, 4.18; N, 19.38; found C, 63.10; H, 4.15; N, 19.40.

2-Amino-7-phenyl- 5-(p-tolyl)-5,8-dihydropyrido[2,3-d]pyrimidin- 4(3H)-one (*4d*)

Yellow solid; mp >300 °C; IR (KBr), ν /cm^{-1} 3400, 3071, 2962, 1650, 1609, 1550,1512; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 2.50 (s, 3H, CH_3), 4.55 (d, 1H, *J* 4.8, CH), 5.05 (d, 1H, *J* 4.8, CH), 5.82 (OH), 6.23 (s, 2H, NH_2), 7.03–7.50 (m, 10H, H–Ar) 8.37 (s, 1H, N–H), 10.21 (s, 1H, NH); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 21.1, 38.5, 88.5, 103.6, 125.9, 127.7, 128.8, 129.0, 147.1, 154.2, 156.8, 162.5, 164.6; Anal. Calcd. for $C_{20}H_{18}N_4O$: C, 72.71; H, 5.49; N, 16.96; found C, 72.68; H, 5.45; N, 16.92.

2-Amino-7-phenyl- 5-(pyridin-4-yl)-5,8-dihydropyrido[2,3-d]pyrimidin -4(3H)-one (*4e*)

Yellow solid; mp >300 °C; IR (KBr) ν /cm^{-1} 3400, 3071, 1650, 1609, 1550, 1512; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 4.64 (d, 1H, *J* 3.0, CH), 5.03 (d, 1H, *J* 3.0, CH), 6.24 (OH), 6.69 (s, 2H, NH_2), 7.26–7.50 (m, 8H, H–Ar), 8.14 (s,1H, H–Ar), 8.50 (m, 2H, H–Ar), 10.48 (s, 1H, NH); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 37.9, 86.8, 101.8, 123.2, 126.2, 128.8, 129.2, 135.8, 137.0, 148.9,149.9, 154.8, 156.7, 162.8; Anal. Calcd. for $C_{18}H_{15}N_5O$: C, 68.13; H, 4.76; N, 22.07; found C, 68.2; H, 4.80; N, 22.02.

2-Amino-5-(naphthalen -2-yl)-7-phenyl-5,8-dihydropyrido[2,3- d]pyrimidin-4(3H)-one (*4f*)

Yellow solid; mp >300 °C; IR (KBr) ν /cm^{-1} 3400, 3071, 1650, 1609, 1550, 1512; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 4.61 (d, 1H, *J* 3.0, CH), 5.03 (d, 1H, *J* 3.0, CH), 5.89 (OH), 6.36 (s, 2H, NH_2), 7–7.78 (12H, m, H–Ar), 8.41 (s, 1 H, NH), 10.42 (s, 1 H, NH); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 40.9, 89.4, 104.2, 125.5, 127.7, 128.6, 128.7, 128.9, 136.4, 137.2, 138.8, 152.8, 157.6, 162.2, 167.0; Anal. Calcd. for $C_{23}H_{18}N_4O$: C, 73.39; H, 4.95; N, 15.29; found C, 73,45.2; H, 4.89; N, 15.20.

2-Amino-5-(furan-2-yl)-7-phenyl-5,8-dihydropyrido [2,3-d]pyrimidin-4(3H)-one (*4g*)

Yellow solid; mp >300 °C; IR (KBr) ν /cm^{-1} 3400, 3071, 1650, 1609, 1550, 1512; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 4.89 (d, 1H, *J* 4.8, CH), 5.16 (d, 1H, *J* 4.8, CH), 5.89 (OH), 6.33 (s, 2H, NH_2), 7.06–7.75 (m, 8H, H–Ar), 8.42 (s, 1H, NH), 10.23 (s, 1H, NH); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 37.7, 89.6, 103.5, 110.0, 117.8, 127.3, 127.7, 128.9, 137.9, 142.1, 146.0, 146.9, 152.2, 158.0, 164.1; Anal. Calcd. for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.61; N, 18.29; found C, 66.56; H, 4.71; N, 18.35.

2-Amino-7-(4-nitrophenyl)-5-phenyl-5,8-dihydropyrido [2,3-d]pyrimidin-4(3H)-one (*4h*)

Yellow solid; mp 295–297 °C; IR (KBr) ν /cm^{-1} 3420, 3073, 1655, 1612, 1552, 1517, 1353; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 4.62 (d, 1H, *J* 5.1, CH), 5.31 (d, 1H, *J* 5.1, CH), 5.98 (OH) 6.64 (s, 2H, NH_2), 7.13–7.40 (m, 6H, H–Ar), 8.18 (d, 2H, *J* 8.4, H–Ar), 8.32 (d, 2H, *J* 8.4, H–Ar), 8.44 (s, 1H, NH), 10.35 (s, 1H, NH); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 37.8, 92.8, 103.3, 126.1, 126.4, 126.6, 128.5, 128.9, 133.0, 150.1, 154.2, 154.2, 159.9, 162.3; Anal. Calcd. for $C_{19}H_{15}N_5O_3$: C, 63.15; H, 4.18; N, 19.38; found C, 63.25; H, 4.08; N, 19.40.

2-Amino-5-phenyl-3,5,6,11-tetrahydro-4H-indeno [2',1':5,6]pyrido[2,3-d]pyrimidin-4-one (*4i*)

Light brown solid; mp >300 °C; IR (KBr) ν /cm^{-1} 3400, 3071, 1650, 1609, 1550, 1512; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 2.73 (d, 2H, *J* 6.0, CH_2), 2.89 (d, 2H, *J* 6.0, CH_2), 4.77 (s, 1H, CH), 5.94 (OH), 6.31 (s, 2H, NH_2) 7.13–7.57 (m, 9H, H–Ar), 8.00 (s, 1H, NH), 10.02 (s, 1H, NH); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 34.5, 35.9, 103.8, 105.4, 126.1, 127.7, 128.5, 128.6, 128.8, 132.4, 149.0, 154.5, 156.8, 162.4; Anal. Calcd. for $C_{20}H_{16}N_4O$: C, 73.15; H, 4.91; N, 17.06; found C, 73.05; H, 4.85; N, 17.20.

2-Amino-5-phenyl-5,11-dihydro-3H-indeno [2',1':5,6]pyrido[2,3-d]pyrimidine-4,6-dione (*4j*)

White solid; mp >300 °C; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 4.89 (s, 1 H, CH), 5.91(OH), 6.27(s, 2H, NH_2), 7.09–7.80(m, 9H, H–Ar), 8.13 (s, 1H, NH), 10.03(s, 1H, NH).

2-Amino-8,8-dimethyl-5-phenyl-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-4,6(3H,7H)-dione (*4k*)

White solid; mp > 300 °C; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 0.84 (s, 3 H, Me), 1.18 (s, 3 H, Me), 1.68–1.92 (m, 2 H, CH_2), 2.69 (s, 2H, CH_2), 4.89 (s, 1H), 5.59 (OH), 6.37 (s, 2 H), 7.18–7.52 (m, 5 H), 8.12 (s, 1 H), 9.87 (NH).

8-Amino-5-phenyl-5,10-dihydropyrido[2,3-d:6,5-d'] dipyrimidine-2,4,6(1H,3H,7H)-trione (*4l*)

White solid; mp >300 °C; IR (KBr) ν /cm^{-1} 3400, 3071, 1650, 1609, 1550, 1512; ^{1}H NMR (300.13 MHz, DMSO-d_6) δ 4.61 (s, 1 H, CH), 5.63 (OH), 6.33 (s, 2H, NH_2), 6.91 (s, NH), 7.17–7.36 (m, 5H, H-Ar), 8.38 (s, 1H, NH), 10.32 (s, 1H, NH), 10.78 (s, 1H, NH); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 43.8, 88.9, 109.2, 127.6, 128.3, 128.4, 133.4, 147.9, 148.9, 150.0, 162.5, 167.0, 167.8; Anal. Calcd. for $C_{15}H_{12}N_6O_3$: C, 55.56; H, 3.73; N, 25.91; found C, 55.46; H, 3.83; N, 25.82.

5,5′-(Phenylmethylene)bis(2,6-diaminopyrimidin -4(3H)-one) (*8*)

White solid; mp 198 °C; IR (KBr) ν /cm^{-1} 3400, 3068, 1652, 1610, 1552, 1515, ^{1}H NMR (300.13 MHz, DMSO-d_6) δ *5.72 (s, 1 H, CH), 6.13 (OH), 7.1–7.5 (m, 5H, H–Ar), 8.12–8.21 (8H, N H_2), 9.38–9.42 (b, 2H, NH).*

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