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A green approach for an efficient preparation of 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles using a TiO_2–SiO_2 nanocomposite catalyst under solvent-free conditions

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Abstract: We report on the preparation of a series of 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles, a new efficient protocol, via the condensation reaction of aromatic aldehydes, malononitrile, and guanidine nitrate using a TiO_2–SiO_2 nanocomposite with a molar ratio of 1 : 1 as a heterogeneous catalyst. The use of a low-cost and reusable catalyst under mild and solvent-free conditions, and simplicity in operation with easier isolation of the products in high to excellent yields are the main advantages of this highly versatile and eco-friendly protocol.

Keywords: 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles; eco-friendly protocol; reusability of catalyst; solvent-free conditions; TiO_2–SiO_2 nanocomposite.

1 Introduction

The utilities of nanoscale metal oxides as heterogeneous catalysts occupy an interesting position in organic reactions owing to their special features such as high surface area and pore sizes as supports [1–4]. Among transition-metal oxide nanoparticles (NPs), nanosized titanium dioxide (TiO_2) NPs have been of considerable interest because of their superior properties such as high catalytic activity, non-toxicity, easily availability, moisture stability, and reusability [5–12]. During recent years, the use of TiO_2 NPs supported on silica shells (TiO_2–SiO_2 nanocomposite) as catalyst has attracted attention due to the improved structural, chemical, electrical, and optical properties [13].

Pyrimidines and their derivatives are of considerable interest as they possess a wide range of biological properties, such as antibacterial [14], antimicrobial [15], antiviral [16], antihypertensive [17], antimalarial [18], and antitumor [19]. In addition, they can be used as integral backbones of several calcium blockers, antihypertensive agents, α-1a-antagonists, and neuropeptide Y antagonists [20].

There are some examples for the syntheses of 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles in the literature via the condensation reaction of aromatic aldehydes, malononitrile, and guanidine hydrochloride or carbonate [21–24]. Although these procedures have their advantages, research for a simple, efficient, and environmentally friendly procedure that afforded the desired products in higher yields is still strongly desired.

In view of the biological significance of pyrimidinones mentioned above and with the fact that TiO_2–SiO_2 nanocomposites make the development of a new catalytic procedure possible for organic transformations under milder reaction conditions, we investigate a TiO_2–SiO_2 nanocomposite as catalyst for the synthesis of a series of 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles. It was found that the TiO_2–SiO_2 nanocomposite is an effective promoter for the synthesis of 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles under solvent-free conditions (Scheme 1).

2 Results and discussion

In continuation of our previous research on the use of nanostructured catalysts for the synthesis of biologically important heterocycles [25, 26], an attempt has been made to synthesize 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles by the reaction of aromatic aldehydes, malononitrile, and guanidine nitrate under solvent-free conditions using a TiO_2–SiO_2 nanocomposite as catalyst at 80°C (Scheme 1).

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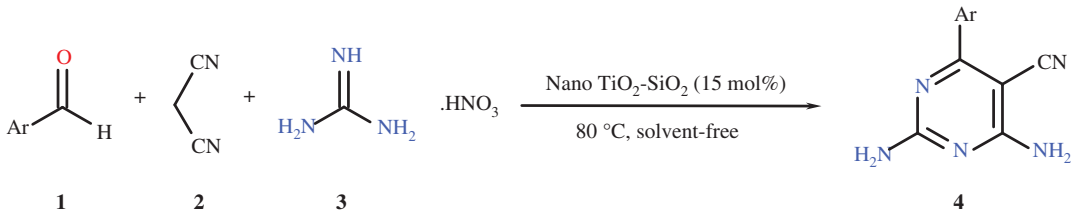

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Scheme 1: Solvent-free synthesis of 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles using a TiO_2–SiO_2 nanocomposite catalyst.

In this work, the TiO_2–SiO_2 nanocomposite was prepared via a simple sol–gel method reported by Nilchi et al. [27]. The XRD pattern of TiO_2–SiO_2 (Fig. 1) could be indexed as the anatase phase in an amorphous silica matrix. The chemical composition of the as-prepared nanocomposite was also determined by X-ray fluorescence (XRF) spectroscopy, and the results show that the molar ratio was 1 : 1.

The morphology and grain size of TiO_2–SiO_2 were investigated by a transmission electron microscopy (TEM) image (Fig. 2). They have a grainy structure with sizes of 5–9 nm.

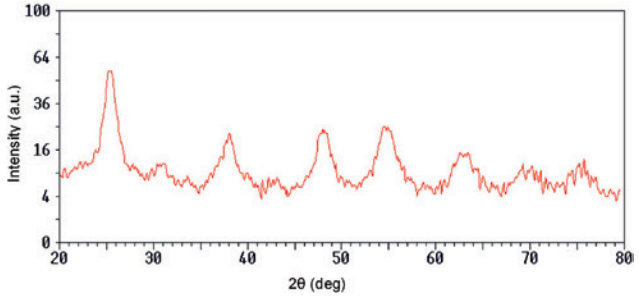


Fig. 1: XRD pattern of the synthesized TiO_2–SiO_2 nanocomposite.

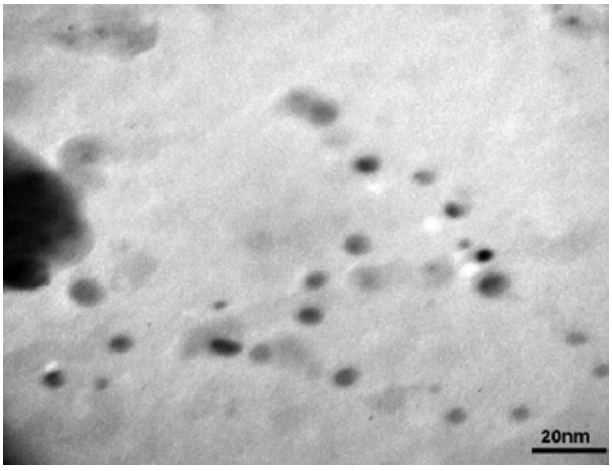


Fig. 2: TEM image of the TiO_2–SiO_2 nanocomposite.

To optimize the reaction conditions, we first tried to seek the efficiency of the TiO_2–SiO_2 nanocomposite catalyst, in the model reaction of 4-chlorobenzaldehyde (**1d**), malononitrile (**2**), and guanidine nitrate (**3**). After 2 h with 10, 15, and 20 mol% of the catalyst, yields of 62%, 94%, and 94%, respectively, were obtained. When the reaction was carried out in the absence of the catalyst, it is notable that, after 5 h, no reaction occurred (Table 1, entries 1–4).

Thus, the next effort was centralized on the evaluation of the catalytic efficiency of the TiO_2–SiO_2 nanocomposite compared with two commercial nanopowders, TiO_2 NPs (10–30 nm, anatase-TiO_2) and SiO_2 NPs (20 nm, nonporous). As shown in Table 1, when the reaction was performed using 20 mol% of the TiO_2 NPs and the SiO_2 NPs alone, the desired product **4d** was obtained in 88% and 84% yields, respectively. On the other hand, the study on the catalytic potential of the TiO_2–SiO_2 nanocomposite showed that the reaction time and the catalyst loading were decreased with higher yield of the product (Table 1, entries 3 and 5, 6).

Increasing the temperature to more than 80°C did not improve the yield (Table 1, entries 3 and 7).

A comparison of the same reaction in various reaction media is also presented in Table 1. Using solvents such as EtOH, CH_2Cl_2, and DMF was less effective as compared to using solvent-free conditions (Table 1, entries 3 and 8–10).

To establish the reusability, the catalyst was recovered by simple filtration using the centrifugation method and reusing it during four subsequent experiments with a moderate decrease in catalytic activity (Fig. 3).

Subsequently, the method was extended to substituted aromatic aldehydes, yielding the corresponding products in high to excellent yields (Table 2). The structures of the compounds **4a–4k** were confirmed by IR, ^{1}H NMR, and ^{13}C NMR spectroscopic data and also by elemental analyses for new compounds.

In our opinion this protocol has some merits in comparison with several previous methods. To demonstrate the superiority of the present work, we compared the yields, conditions, scope, and generality of this method for the synthesis of 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles with the literature procedures (Table 3).

Table 1: Optimization of the reaction conditions using the model reaction of 4-chlorobenzaldehyde (**1d**), malononitrile (**2**), and guanidine nitrate (**3**) under different conditions.

Entry	Catalyst (mol% with respect to TiO_2)	Solvent	Temp. (°C)	Time (h)	Yield (%)[a]
1	No catalyst	None	80	5	Trace
2	Nano TiO_2–SiO_2 (10%)	None	80	2	62
3	Nano TiO_2–SiO_2 (15%)	None	80	2	94
4	Nano TiO_2–SiO_2 (20%)	None	80	2	94
5	Nano TiO_2 (20%)	None	80	2.5	88
6	Nano SiO_2 (20%)	None	80	3	84
7	Nano TiO_2–SiO_2 (15%)	None	100	2	95
8	Nano TiO_2–SiO_2 (15%)	EtOH	Reflux	3	82
9	Nano TiO_2–SiO_2 (15%)	CH_2Cl_2	Reflux	4	80
10	Nano TiO_2–SiO_2 (15%)	DMF	Reflux	2	87

[a]Isolated yield.

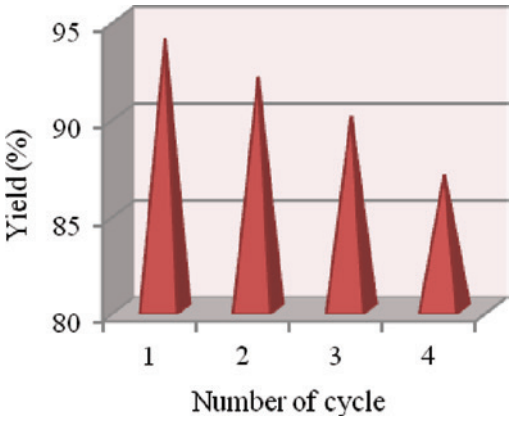


Fig. 3: Reusability of the TiO_2–SiO_2 nanocatalyst.

Table 2: Synthesis of a series of 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles using a TiO_2–SiO_2 nanocomposite catalyst.

Product	Ar	Yield (%)[a,b]	M.p. (°C)	
			Obsd.	Lit.
4a	C_6H_5	90	238–240	237–239 [24]
4b	4-Br-C_6H_4	92	259–261	260–262 [24]
4c	3-Cl-C_6H_4	91	251–253	253–255 [24]
4d	4-Cl-C_6H_4	94	266–267	265–266 [24]
4e	2,4-Cl_2-C_6H_3	92	233–235	–
4f	3-HO-C_6H_4	90	268–270	–
4g	4-CH_3O-C_6H_4	93	234–235	236–238 [24]
4h	4-CH_3-C_6H_4	91	256–258	255–257 [24]
4i	4-NO_2-C_6H_4	94	244–246	–
4j	Pridine-4-yl	95	230–232	–
4k	Thiophen-2-yl	93	222–224	–

[a]Yields refer to those of pure isolated products characterized by IR, ^1H, and ^{13}C NMR spectral data and by elemental analyses.
[b]In all cases, the reaction mixture was stirred for 2 h at 80°C.

A suggested mechanism for the reaction is provided in Scheme 2. This pathway involves the TiO_2 NP participation in the formation of alkene **7** which comes from a Knoevenagel condensation between aromatic aldehydes **1** and malononitrile **2**, via intermediate **5** and **6**. Guanidine nitrate **3** is then added to alkene **7** to generate the Michael adduct **8**, which further undergoes intermolecular cyclization and then aromatization to give the product **4**.

3 Conclusions

In conclusion, we found a novel solvent-free approach for the synthesis of 2,4-diamino-6-aryl-5-pyrimidinecarbonitrile derivatives. Meanwhile the new method also expands the application of the TiO_2–SiO_2 nanocomposite in organic synthesis. Compared with previous methods, this method has the advantages of high yields, mild reaction conditions, short reaction time, easy work-up, inexpensive reagents, and environmentally friendly procedure.

4 Experimental section

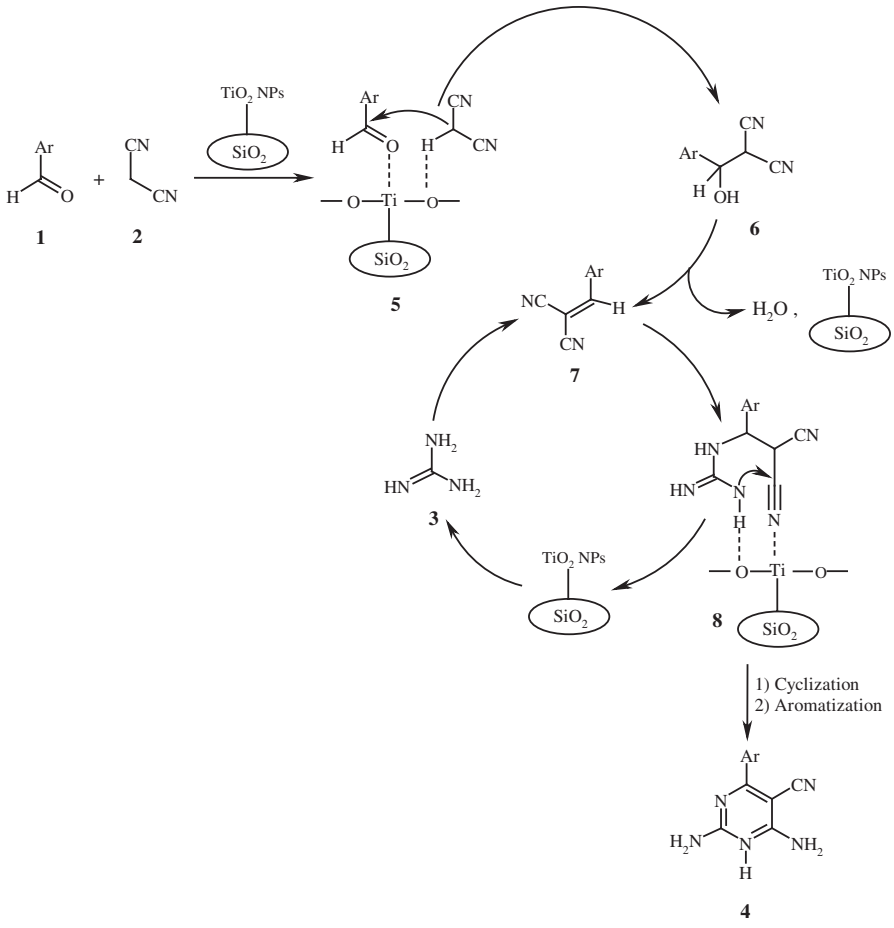
4.1 Materials and methods

All chemicals used in this work were purchased from Merck and Fluka in high purity (Kimiaexir Chemical Company, Tehran, Iran). Melting points were determined with Electrothermal 9100 apparatus (East Tehran Branch, Islamic Azad University, Tehran, Iran). FT-IR spectra were obtained using a Bruker Equinox 55 Golden Gate Micro-ATR spectrometer (Chemistry and Chemical Engineering Research Center of Iran, Tehran, Iran). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX-500 AVANCE at 500 and 125 MHz, respectively, using tetramethylsilane (TMS) as internal standard and [D_6]dimethyl sulfoxide

Table 3: Comparison of the catalytic efficiency of the TiO_2–SiO_2 nanocomposite with various known catalysts for the preparation of 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles.

Conditions	Ar	Yield (%)[a]	References
Aromatic aldehydes (1 mmol), malononitrile (1.2 mmol), guanidine hydrochloride (1.2 mmol), potassium carbonate (1.0 g), and a pinch of TBAB[b] in distilled water (30 mL), at reflux, 3–4 h	C_6H_5, 3-Cl-C_6H_4, 4-*N*,*N*-$(CH_3)_2$-C_6H_4, 2-HO-C_6H_4, 4-HO-C_6H_4, 3,4-$(CH_3O)_2$-C_6H_3, 4-CH_3O-C_6H_4	63–75	[21]
Aromatic aldehydes (2 mmol), malononitrile (2 mmol), guanidine hydrochloride (2 mmol), and $NaOCH_3$ (2 mmol) in H_2O (50 mL) and EtOH (5 mL), at reflux, 3–5 h	C_6H_5, 4-Br-C_6H_4, 4-Cl-C_6H_4, 4-CH_3-C_6H_4	64–82	[22]
Aromatic aldehydes (2 mmol), malononitrile (2 mmol), guanidine hydrochloride (2 mmol), and triethylamine (3–4 drops) in toluene (5 mL), under 300 W MWI, 25–45 min	C_6H_5, 4-Br-C_6H_4, 4-Cl-C_6H_4, 4-CH_3-C_6H_4	85–96	[22]
Aromatic aldehydes (2 mmol), malononitrile (2 mmol), guanidine hydrochloride (2 mmol), and MgO (0.25 g) in CH_3CN (5 mL), at reflux, 8–22 min	C_6H_5, 4-Br-C_6H_4, 4-Cl-C_6H_4, 3-F-C_6H_4, 4-F-C_6H_4, 4-CH_3-C_6H_4, 4-CF_3-C_6H_4	86–96	[23]
Aromatic aldehydes (2 mmol), malononitrile (3 mmol), guanidine carbonate (1 mmol), and NaOH (1.0 eq) under solvent-free conditions, at 70°C, 4 h	C_6H_5, 4-Br-C_6H_4, 3-Cl-C_6H_4, 4-Cl-C_6H_4, 3,4-Cl_2-C_6H_3, 4-F-C_6H_4, 4-CH_3O-C_6H_4, 4-CH_3-C_6H_4, 3,4-$(CH_3)_2$-C_6H_3	80–92	[24]
Aromatic aldehydes (1 mmol), malononitrile (1.2 mmol), guanidine nitrate (1.2 mmol), and TiO_2–SiO_2 nanocomposite (21 mg, 15 mol%) under solvent-free conditions, at 80°C, 2 h	C_6H_5, 4-Br-C_6H_4, 3-Cl-C_6H_4, 4-Cl-C_6H_4, 2,4-Cl_2-C_6H_3, 3-HO-C_6H_4, 4-CH_3O-C_6H_4, 4-CH_3-C_6H_4, 4-NO_2-C_6H_4, pridine-4-yl, thiophen-2-yl	90–95	This work

[a]Isolated yield.
[b]TBAB, tetrabutylammonium bromide.



Scheme 2: Proposed mechanism for the synthesis of 2,4-diamino-6-aryl-5-pyrimidinecarbonitriles catalyzed by a TiO_2–SiO_2 nanocomposite.

(DMSO) as a solvent (Sharif University of Technology, Tehran, Iran). Elemental analyses were carried out using a Foss-Heraeus CHN-O-Rapid analyzer (Polymer and Petrochemical Institute, Tehran, Iran). The TEM image of the catalyst was obtained on a Philips EM208 transmission electron microscope under acceleration (Nuclear Science and Technology Research Institute AEOI, Tehran, Iran). Powder X-ray diffraction data were determined on a Philips, X'Pert diffractometer using CuK_α radiation ($\lambda = 1.54$ Å) (Nuclear Science and Technology Research Institute AEOI). The composition analysis of the catalyst was carried out by XRF spectroscopy using Oxford ED 2000 equipment (Nuclear Science and Technology Research Institute AEOI).

4.2 General procedure for the preparation of TiO_2–SiO_2 nanocomposite catalyst

First, titanium tetrachloride (2 mL) was added dropwise into the deionized water (200 mL) in an ice-water bath with strong magnetic stirring. After the hydrolysis was completed, the released HCl was neutralized by adding dilute NH_4OH to adjust the pH to 7. The produced solid was filtered and washed with distilled water. The precipitate was dispersed into a 0.3 M HNO_3 aqueous solution (200 mL) to remove all the chloride ions. The mixture was then refluxed under strong stirring at 70°C for 16 h, as the titania sol was prepared. Tetraethyl orthosilicate (25 mL) was added dropwise into the above sol and stirred at 70°C for about 0.5 h. Finally, the TiO_2–SiO_2 nanocomposite powder was filtered and washed with distilled water and then dried in air at ambient temperature [27].

4.3 General procedure for the synthesis of compounds 4a–4k

A mixture of aromatic aldehydes **1** (1 mmol), malononitrile (**2**, 1.2 mmol), guanidine nitrate (**3**, 1.2 mmol), and TiO_2–SiO_2 nanocomposite (21 mg, 15 mol%) was stirred at 80°C for about 2 h. The progress of the reaction was monitored by thin-layer chromatography (acetone–petroleum ether, 1 : 3). Upon completion of the reaction, hot ethanol (5 mL) was added to the reaction mixture, and the catalyst was filtered and dried in air at ambient temperature for reuse. The organic solution was poured into the ice-cold water (5 mL) and the solid was removed by filtration and then recrystallized from EtOH–H_2O to give the pure product in high yield.

4.4 Selected spectroscopic and physical data

4.4.1 2,4-Diamino-6-phenyl-5-pyrimidinecarbonitrile (4a)

Yield: 0.190 g (90%), m.p. 238–240°C (lit: 237–239°C [24]). – IR (KBr, cm^{-1}): ν_{max} 3328, 3196, 3011, 2945, 2388, 2199, 1623, 1587. – ^{1}H NMR: $\delta = 7.12$ (s, 2 H, NH_2), 7.25 (s, 2 H, NH_2), 7.52 (m, 3 H, HAr), 7.73 (m, 2 H, HAr) ppm. – ^{13}C NMR: $\delta = 74.5$ (*C*–CN), 118.9 (CN), 122.5 (2 CH), 127.4 (CH), 130.3 (2 CH), 139.4 (C), 164.6 (C–NH_2), 169.1 (C–NH_2), 170.9 (C) ppm. – Analysis for $C_{11}H_9N_5$ (211.23): calcd. C 62.55, H 4.29, N 33.16; found C 62.44, H 4.21, N 33.29%.

4.4.2 2,4-Diamino-6-(4-bromophenyl)-5-pyrimidinecarbonitrile (4b)

Yield: 0.267 g (92%), m.p. 259–261°C (lit: 260–262°C [24]). – IR (KBr, cm^{-1}): ν_{max} 3501, 3411, 3376, 3143, 2205, 1681, 1616, 1546. – ^{1}H NMR: $\delta = 7.03$ (s, 2 H, NH_2), 7.16 (s, 2 H, NH_2), 7.71 (br s, 4 H, HAr) ppm. – ^{13}C NMR: $\delta = 79.3$ (*C*–CN), 120.1 (CN), 131.1 (2 CH), 134.7 (2 CH), 136.8 (CH), 140.2 (C), 165.4 (C–NH_2), 167.0 (C–NH_2), 168.9 (C) ppm. – Analysis for $C_{11}H_8BrN_5$ (290.12): calcd. C 45.54, H 2.78, N 24.14; found C 45.40, H 2.87, N 24.24%.

4.4.3 2,4-Diamino-6-(3-chlorophenyl)-5-pyrimidinecarbonitrile (4c)

Yield: 0.224 g (91%), m.p. 251–253°C (lit: 253–255°C [24]). – IR (KBr, cm^{-1}): ν_{max} 3489, 3420, 3378, 3126, 2371, 2200, 1623, 1530. – ^{1}H NMR: $\delta = 7.10$–7.24 (br s, 4 H, 2 NH_2), 7.53 (t, 1 H, $J = 7.6$ Hz, HAr), 7.59 (d, 1 H, $J = 7.4$ Hz, HAr), 7.74 (d, 1 H, $J = 8.0$ Hz, HAr), 7.79 (s, 1 H, HAr) ppm. – ^{13}C NMR: $\delta = 80.4$ (*C*–CN), 120.4 (CN), 128.5 (CH), 130.1 (CH), 132.8 (CCl), 133.7 (CH), 137.1 (CH), 138.6 (C), 163.4 (C–NH_2), 166.8 (C–NH_2), 170.3 (C) ppm. – Analysis for $C_{11}H_8ClN_5$ (245.67): calcd. C 53.78, H 3.28, N 28.51; found C 53.85, H 3.40, N 28.62%.

4.4.4 2,4-Diamino-6-(4-chlorophenyl)-5-pyrimidinecarbonitrile (4d)

Yield: 0.231 g (94%), m.p. 266–267°C (lit: 265–266°C [24]). – IR (KBr, cm^{-1}): ν_{max} 3496, 3431, 3345, 2968, 2450, 2203, 1618, 1525. – ^{1}H NMR: $\delta = 7.04$ (s, 2 H, NH_2), 7.13 (s, 2 H, NH_2), 7.56 (d, 2 H, $J = 8.6$ Hz, HAr), 7.77 (d, 2 H, $J = 8.6$ Hz, HAr) ppm. – ^{13}C NMR: $\delta = 75.5$ (*C*–CN), 118.7 (CN), 129.0 (2 CH), 133.4 (CCl), 136.1 (2 CH), 139.0 (C), 163.2 (C–NH_2), 165.9 (C–NH_2),

170.4 (C) ppm. – Analysis for $C_{11}H_8ClN_5$ (245.67): calcd. C 53.78, H 3.28, N 28.51; found C 53.43, H 3.16, N 28.08%.

4.4.5 2,4-Diamino-6-(2,4-dichlorophenyl)-5-pyrimidinecarbonitrile (4e)

Yield: 0.258 g (92%), m.p. 233–235°C. – IR (KBr, cm^{-1}): ν_{max} 3427, 3376, 3184, 2360, 2194, 1675, 1545. – ^1H NMR: $\delta = 7.01$ (s, 2 H, NH_2), 7.14 (s, 2 H, NH_2), 7.46 (m, 2 H, HAr), 7.76 (d, 1 H, $J = 7.0$ Hz, HAr) ppm. – ^{13}C NMR: $\delta = 74.1$ (*C*–CN), 119.2 (CN), 123.0 (CH), 131.3 (CH), 134.3 (CCl), 136.2 (CH), 138.8 (C), 140.7 (CCl), 162.8 (C–NH_2), 166.6 (C–NH_2), 171.4 (C) ppm. – Analysis for $C_{11}H_7Cl_2N_5$ (280.12): calcd. C 47.17, H 2.52, N 25.00; found C 47.00, H 2.62, N 24.91%.

4.4.6 2,4-Diamino-6-(3-hydroxyphenyl)-5-pyrimidinecarbonitrile (4f)

Yield: 0.205 g (90%), m.p. 268–270°C. – IR (KBr, cm^{-1}): ν_{max} 3426, 3351, 3268, 3197, 2436, 2361, 2193, 1656, 1526. – ^1H NMR: $\delta = 6.92$ (br s, 4 H, 2 NH_2), 7.78 (m, 1 H, HAr), 7.88 (d, 1 H, $J = 7.5$ Hz, HAr), 8.24 (d, 1 H, $J = 1.6$ Hz, HAr), 8.34 (d, 1 H, $J = 8.2$ Hz, HAr), 9.37 (s, 1 H, OH) ppm. – ^{13}C NMR: $\delta = 76.7$ (*C*–CN), 115.9 (CH), 118.2 (CH), 118.8 (CH), 119.3 (CH), 119.4 (CN), 139.3 (C), 158.4 (COH), 163.8 (C–NH_2), 166.0 (C–NH_2), 170.4 (C) ppm. – Analysis for $C_{11}H_9N_5O$ (227.23): calcd. C 58.15, H 3.99, N 30.82; found C 58.02, H 3.87, N 30.74%.

4.4.7 2,4-Diamino-6-(4-methoxyphenyl)-5-pyrimidinecarbonitrile (4g)

Yield: 0.224 g (93%), m.p. 234–235°C (lit: 236–238°C [24]). – IR (KBr, cm^{-1}): ν_{max} 3487, 3416, 3381, 2950, 2206, 1598, 1531. – ^1H NMR: $\delta = 3.82$ (s, 3 H, OCH_3), 7.10–7.21 (br s, 4 H, 2 NH_2), 7.05 (d, 2 H, $J = 8.4$ Hz, HAr), 7.76 (d, 2 H, $J = 8.4$ Hz, HAr) ppm. – ^{13}C NMR: $\delta = 55.6$ (OCH_3), 80.1 (*C*–CN), 119.5 (CN), 115.7 (2 CH), 136.4 (2 CH), 138.0 (C), 159.6 (*C*OCH_3), 162.2 (C–NH_2), 167.5 (C–NH_2), 171.3 (C) ppm. – Analysis for $C_{12}H_{11}N_5O$ (241.25): calcd. C 59.74, H 4.60, N 29.03; found C 59.82, H 4.68, N 29.89%.

4.4.8 2,4-Diamino-6-(4-methylphenyl)-5-pyrimidinecarbonitrile (4h)

Yield: 0.224 g (91%), m.p. 256–258°C (lit: 255–257°C [24]). – IR (KBr, cm^{-1}): ν_{max} 3442, 3417, 3359, 3168, 2207, 1691, 1616, 1535. – ^1H NMR: $\delta = 2.35$ (s, 3 H, CH_3), 7.03–7.10 (br s, 4 H, 2 NH_2), 7.29 (d, 2 H, $J = 7.9$ Hz, HAr), 7.67 (d, 2 H, $J = 7.9$ Hz, HAr) ppm. – ^{13}C NMR: $\delta = 20.6$ (CH_3), 78.2 (*C*–CN), 120.2 (CN), 125.2 (2 CH), 136.1 (2 CH), 138.5 (*C*CH_3), 139.2 (C), 164.3 (C–NH_2), 166.9 (C–NH_2), 170.8 (C) ppm. – Analysis for $C_{12}H_{11}N_5$ (225.25): calcd. C 63.99, H 4.92, N 31.09; found C 63.78, H 4.74, N 31.20%.

4.4.9 2,4-Diamino-6-(4-nitrophenyl)-5-pyrimidinecarbonitrile (4i)

Yield: 0.241 g (94%), m.p. 244–246°C. – IR (KBr, cm^{-1}): ν_{max} 3508, 3442, 3292, 3018, 2402, 2226, 1620, 1528, 1505, 1380. – ^1H NMR: $\delta = 7.09$ (s, 2 H, NH_2), 7.20 (s, 2 H, NH_2), 7.45 (d, 2 H, $J = 8.4$ Hz, HAr), 8.06 (d, 2 H, $J = 8.4$ Hz, HAr) ppm. – ^{13}C NMR: $\delta = 78.3$ (C–CN), 119.6 (CN), 123.4 (2 CH), 134.0 (2 CH), 142.3 (C), 148.7 (CNO_2), 165.3 (C–NH_2), 168.4 (C–NH_2), 171.2 (C) ppm. – Analysis for $C_{11}H_8N_6O_2$ (256.22): calcd. C 51.57, H 3.15, N 32.80; found C 51.72, H 3.24, N 32.66%.

4.4.10 2,4-Diamino-6-(pyridine-4-yl)-5-pyrimidinecarbonitrile (4j)

Yield: 0.202 g (95%), m.p. 230–231°C. – IR (KBr, cm^{-1}): ν_{max} 3451, 3364, 3275, 3192, 2224, 1661, 1646, 1543. – ^1H NMR: $\delta = 6.95$–7.07 (br s, 4 H, 2 NH_2), 7.48 (d, 2 H, $J = 7.9$ Hz, HAr), 8.26 (d, 2 H, $J = 7.9$ Hz, HAr) ppm. – ^{13}C NMR: $\delta = 80.1$ (C–CN), 119.8 (CN), 125.8 (2 CH), 141.3 (C), 146.5 (2 CH), 163.4 (C–NH_2), 168.2 (C–NH_2), 169.6 (C) ppm. – Analysis for $C_{10}H_8N_6$ (212.21): calcd. C 56.60, H 3.80, N 39.60; found C 56.51, H 3.65, N 39.49%.

4.4.11 2,4-Diamino-6-(thiophen-2-yl)-5-pyrimidinecarbonitrile (4k)

Yield: 0.202 g (93%), m.p. 222–224°C. – IR (KBr, cm^{-1}): ν_{max} 3460, 3379, 3172, 3025, 2218, 1654, 1536, 1448, 1412. – ^1H NMR: $\delta = 6.79$ (m, 2 H, HAr), 7.00–7.08 (br s, 4 H, 2 NH_2), 7.18 (m, 1 H, HAr) ppm. – ^{13}C NMR: $\delta = 75.0$ (*C*–CN), 119.4 (CN), 120.5 (CH), 128.6 (CH), 134.9 (CH), 138.7 (C), 167.0 (C–NH_2), 168.8 (C–NH_2), 169.5 (C) ppm. – Analysis for $C_9H_7N_5S$ (217.25): calcd. C 49.76, H 3.25, N 32.24; found C 49.65, H 3.44, N 32.10%.

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