An Efficient Synthesis of 4-Naphthylpyrimidin-2-amine Derivatives under Solvent-Free Conditions

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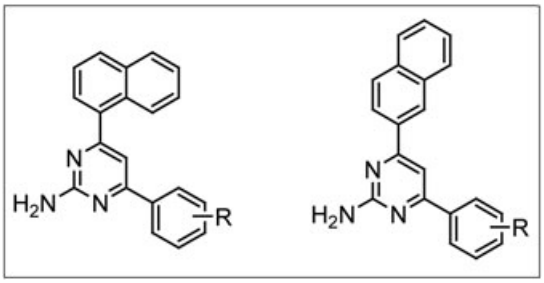

A simple, efficient, and mild protocol for the synthesis of 4-naphthylpyrimidin-2-amine derivatives under solvent-free conditions by the reaction of aromatic aldehydes (or 1-naphthaldehyde), 2-acetylnaphthalene (or aromatic ketones), guanidine carbonate, and sodium hydroxide was reported. The advantages of this protocol include short reaction time, mild reaction conditions, easy workup, high yields, and environmental friendliness.

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INTRODUCTION

In recent years, pyrimidines and their derivatives have received considerable attention in organic chemistry because of their biological activities [1]. Substituted pyrimidines are important compounds of drugs and other bioactive molecules [2]. They display a wide range of pharmacological activities [3–6]. For example, aminopyrimidine derivatives have displayed interesting antibacterial, antitumor, and HIV-I inhibiting activities [7]. Because of their interesting activity as biological agents, considerable attention has been focused on synthesizing this class of compounds.

The various methods of synthesis of aminopyrimidines were reported [8–10]. 2-Aminopyrimidines were prepared previously by the reaction of substituted benzylideneacetophenones with guanidine under reflux in ethanol [11,12]. In 2007, Goswami et al. reported the synthesis of functionalized pyrimidines with the microwave-expedited method. This method involves column chromatography, which would consume a lot of solvents and time that lead to a relatively low yields. Meanwhile, it takes microwave as its reaction condition, which would give off radiation that is harmful to our health [13]. A recent report described the preparation of 2,5,6-substitued pyrimidines via MgI_2-mediated MBH reaction [14]. In this report, it involves complex catalysts and some toxic solvents as reaction medium. What's more, the synthetic procedure was multistep and some air-sensitive reactions must be carried out under an atmosphere of argon. Nagarajan and coworkers reported the synthesis of 2-amino-4-(1-naphthyl)-6-arylpyrimidines by the three-step reaction, which should undergo the process of acetylation, Claisen-Schmidt Condensation, Michael addition, and cyclization [15]. Because of its multistep process, the after-treatment was very complex. In addition, the catalyst aluminum chloride used in the acetylation must be anhydrous. In 2010, Gopalakrishnan and coworkers reported the synthesis of 2-morpholino-*N*-(4,6-diarylpyrimidin-2-yl)acetamides. In this report, it not only suffered the similar drawbacks mentioned above but also experienced long-reaction time [16]. On the whole, most of these methods are associated with different drawbacks such as long reaction time, low yields, strongly alkalic conditions, use of toxic reagents, and the requirement of an additional microwave oven. Hence, it is important to develop a simple and convenient approach for the preparation of pyrimidin-2-amine derivatives.

With the development of organic synthesis and environmental concerns, developing a clean synthetic procedure has become increasingly urgent. In this context, organic reactions under solvent-free conditions are ideal protocols for the development of environmental friendly and economical advantageous chemical processes. Nowadays, there has been an upsurge of interest in synthesizing compounds in solvent-free environment [17–20]. When compared with the methods used in the solvent, the solvent-free approach provided more advantages such as higher yields, short reaction time, and easy workup. Multicomponent reactions (MCRs) have proven

to be a valuable protocol in medicinal chemistry, drug design, and drug discovery because of their simplicity, efficiency, and high selectivity. It must be an ideal process for multicomponent reactions, which can be carried out under solvent-free conditions. Herein, we report the synthesis of 4-naphthylpyrimidin-2-amine derivatives via a simple, green, one-pot, three-component reaction under solvent-free conditions.

RESULTS AND DISCUSSION

First, we carried out the reaction of aromatic aldehyde **1**, 2-acetylnaphthalene, guanidine carbonate **3**, and sodium hydroxide in a mortar (Scheme 1). The mixture was ground and then heated at 70°C under solvent-free conditions for about 30 min and the reactions could be completed, and the corresponding 4-(naphthalen-2-yl)-6-arylpyrimidin-2-amine derivatives were obtained in excellent yields (Table 1).

To explore the scope of the reaction, we tried the reaction of naphthaldehyde, aromatic ketones, and guanidine carbonate. The corresponding 4-(naphthalen-1-yl)-6-arylpyrimidin-2-amine derivatives were obtained in good yields (Scheme 2). The results were summarized in Table 2. The structures of all the products were confirmed by spectroscopic data, particularly ^{1}H NMR and HRMS.

In conclusion, we have developed an efficient and simple three-component reaction for the synthesis of 4-naphthylpyrimidin-2-amine derivatives. This method has the advantages of operational simplicity, high efficiency, low cost, and mild reaction conditions. Furthermore, the reaction was performed in good yields within short reaction times. It is notable that we carried out the reaction use the substrate with high steric effect under solvent-free conditions. Starting materials are also inexpensive and commercially available.

EXPERIMENTAL

Melting points were determined on XT-5 microscopic melting-point apparatus and were uncorrected. IR spectra were recorded on a FTIR-8101 spectrometer. ^{1}H-NMR spectra were obtained from solution in DMSO-d_6 with Me_4Si as internal standard using a Bruker-400 spectrometer. Microanalyses were carried out using a Perkin-Elmer 2400 II analyzer. HRMS spectra were obtained with a Bruker micrOTOF-Q 134 instrument.

General procedure for the synthesis of 4-naphthylpyrimidin-2-amine derivatives. A mixture of aromatic aldehydes (or 1-naphthaldehyde) **1** (2 mmol), 2-acetylnaphthalene (or aromatic ketones) **2** (2 mmol), guanidine carbonate **3** (3 mmol), and sodium hydroxide (2 mmol) was ground in a mortar. Then, the mixture was transferred to a round bottom flask. The mixture was heated at ~70°C over the course of 30 min. After the reaction was completed, the reaction mixture was poured into water, and then washed with water thoroughly. The product was filtered, dried, and recrystallized from 95% ethanol.

Table 1

The results of synthesis of 4-(naphthalen-2-yl)-6-arylpyrimidin-2-amine.

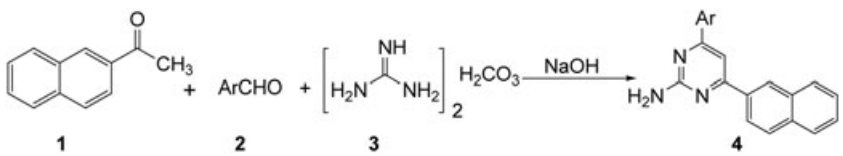
Entry	Ar	Products	Yields (%)
1	4-$CH_3C_6H_4$	**4a**	91
2	4-$CH_3OC_6H_4$	**4b**	81
3	3,4-$(CH_3O)_2C_6H_3$	**4c**	87
4	4-FC_6H_4	**4d**	90
5	4-BrC_6H_4	**4e**	86
6	4-ClC_6H_4	**4f**	88
7	2,4-$Cl_2C_6H_3$	**4g**	89
8	3,4-$Cl_2C_6H_3$	**4h**	83

4-(Naphthalen-2-yl)-6-p-tolylpyrimidin-2-amine (4a). M.p. 154–156°C; IR (KBr, ν, cm^{-1}): 3326, 3204, 3051, 1645, 1601, 1567, 1536, 1509, 1457, 1363, 1222, 1298, 1185, 1114, 862, 811, 759, 592 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.41 (3H, s, CH_3), 6.77 (2H, s, NH_2), 7.36 (2H, d, J = 8.0 Hz, ArH), 7.60 (2H, dd, J = 3.2 Hz, J = 6.4 Hz, ArH), 7.87 (1H, s, ArH), 8.00 (1H, t, J = 3.2 Hz, ArH), 8.06 (2H, t, J = 8.0 Hz, ArH), 8.18 (2H, d, J = 8.4 Hz, ArH), 8.36 (1H, dd, J = 1.2 Hz, J = 1.6 Hz, ArH), 8.84 (1H, s, ArH); Anal. Calcd. for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 81.22; H, 5.57; N, 13.40. HRMS m/z calculated for $C_{21}H_{17}N_3$ $[M + Na]^+$: 334.1320, found: 334.1322.

4-(4-Methoxyphenyl)-6-(naphthalen-2-yl)pyrimidin-2-amine (4b). M.p. 143–145°C; IR (KBr, ν, cm^{-1}): 3323, 3196, 3055, 1645, 1605, 1568, 1537, 1510, 1439, 1363, 1298, 1248, 1176, 1031, 815, 752, 669, 581, 561 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.86 (3H, s, OCH_3), 6.73 (2H, s, NH_2), 7.10 (2H, d, J = 8.8 Hz, ArH), 7.60 (2H, dd, J = 3.2 Hz, J = 6.4 Hz, ArH), 7.84 (1H, s, ArH), 7.98–8.01 (1H, m, ArH), 8.04–8.08 (2H, m, ArH), 8.25 (2H, d, J = 8.8 Hz, ArH), 8.35 (1H, d, J = 8.8 Hz, ArH), 8.83 (1H, s, ArH); Anal. Calcd. for $C_{21}H_{17}N_3O$: C, 77.04; H, 5.23; N, 12.84. Found: C, 77.22; H, 5.19; N, 12.69. HRMS m/z calculated for $C_{21}H_{17}N_3O$ $[M + Na]^+$: 350.1269, found: 350.1276.

4-(3,4-Dimethoxyphenyl)-6-(naphthalen-2-yl)pyrimidin-2-amine (4c). M.p. 140–141°C; IR (KBr, ν, cm^{-1}): 3320, 3198, 3011, 1625, 1576, 1541, 1504, 1439, 1412, 1333, 1270, 1236, 1220, 1175, 1123, 1026, 817, 794, 754, 741, 669 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.88 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 6.73 (2H, s, NH_2), 7.17 (1H, d, J = 8.4 Hz, ArH), 7.65 (2H, dd, J = 2.0 Hz, J = 4.0 Hz, ArH), 7.82 (1H, d, J = 2.0 Hz, ArH), 7.92–7.97 (2H, m, ArH), 8.09–8.13 (2H, m, ArH), 8.33 (2H, dd, J = 1.6 Hz, J = 8.4 Hz, ArH), 8.85 (1H, s, ArH); Anal.

Scheme 1.



Scheme 2.

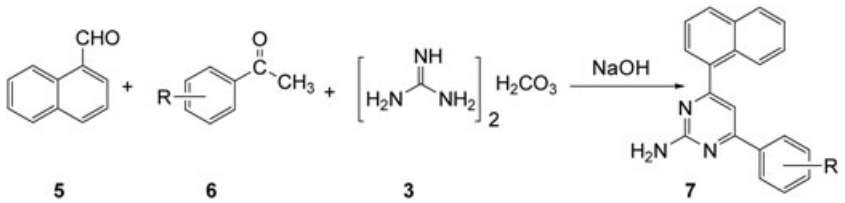


Table 2

The results of synthesis of 4-(naphthalen-1-yl)- 6-arylpyrimidin-2-amine

Entry	R	Products	Yields (%)
1	H	**7a**	91
2	4-CH_3	**7b**	88
3	4-CH_3O	**7c**	90
4	2,4-$(CH_3)_2$	**7d**	81
5	3-Cl	**7e**	89
6	2,4-Cl_2	**7f**	86

Calcd. for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76. Found: C, 73.82; H, 5.40; N, 11.89. HRMS *m/z* calculated for $C_{22}H_{19}N_3O_2$ $[M + Na]^+$: 380.1375, found: 380.1389.

4-(4-Fluorophenyl)-6-(naphthalen-2-yl)pyrimidin-2-amine (4d). M.p. 156–157°C; IR (KBr, ν, cm^{-1}): 3327, 3208, 1645, 1600, 1570, 1540, 1508, 1456, 1372, 1330, 1221, 1158, 1100, 877, 851, 812, 763, 751, 572, 562, 508 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.83 (2H, s, NH_2), 7.38 (2H, t, *J* = 8.8 Hz, ArH), 7.60–7.63 (2H, m, ArH), 7.90 (1H, s, ArH), 8.00 (1H, t, *J* = 3.2 Hz, ArH), 8.05–8.08 (2H, m, ArH), 8.33–8.38 (3H, m, ArH), 8.85 (1H, s, ArH); Anal. Calcd. for $C_{20}H_{14}FN_3$: C, 76.18; H, 4.47; N, 13.33. Found: C, 76.30; H, 4.51; N, 13.42. HRMS *m/z* calculated for $C_{20}H_{14}FN_3$ $[M + Na]^+$: 338.1069, found: 338.1070.

4-(4-Bromophenyl)-6-(naphthalen-2-yl)pyrimidin-2-amine (4e). M.p. 180–181°C; IR (KBr, ν, cm^{-1}): 3303, 3187, 3051, 1633, 1592, 1579, 1541, 1491, 1454, 1363, 1340, 1225, 1104, 1072, 1012, 856, 845, 806, 780, 748 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.87 (2H, s, NH_2), 7.61 (2H, dd, *J* = 3.6 Hz, *J* = 3.2 Hz, ArH), 7.76 (2H, d, *J* = 8.8 Hz, ArH), 7.92 (1H, s, ArH), 8.00 (1H, t, *J* = 3.2 Hz, ArH), 8.05–8.08 (2H, m, ArH), 8.24 (2H, d, *J* = 8.4 Hz, ArH), 8.36 (1H, d, *J* = 8.8 Hz, ArH), 8.85 (1H, s, ArH); Anal. Calcd. for $C_{20}H_{14}BrN_3$: C, 63.84; H, 3.75; N, 11.17. Found: C, 63.67; H, 3.81; N, 11.12. HRMS *m/z* calculated for $C_{20}H_{14}BrN_3$ $[M + Na]^+$: 398.0269, found: 398.0272.

4-(4-Chlorophenyl)-6-(naphthalen-2-yl)pyrimidin-2-amine (4f). M.p. 165–167°C; IR (KBr, ν, cm^{-1}): 3485, 3302, 3186, 1634, 1581, 1568, 1510, 1494, 1457, 1362, 1340, 1225, 1200, 1093, 1015, 883, 856, 804, 782, 748 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.87 (2H, s, NH_2), 7.60–7.64 (4H, m, ArH), 7.92 (1H, s, ArH), 8.00 (1H, dd, *J* = 2.4 Hz, *J* = 3.6 Hz, ArH), 8.05–8.08 (2H, m, ArH), 8.31 (2H, d, *J* = 8.4 Hz, ArH), 8.36 (1H, d, *J* = 8.4 Hz, ArH), 8.85 (1H, s, ArH); Anal. Calcd. for $C_{20}H_{14}ClN_3$: C, 72.40; H, 4.25; N, 12.66. Found: C, 72.60; H, 4.19; N 12.71. HRMS *m/z* calculated for $C_{20}H_{14}ClN_3$ $[M + Na]^+$: 354.0774, found: 354.0778.

4-(2,4-Dichlorophenyl)-6-(naphthalen-2-yl)pyrimidin-2-amine (4g). M.p. 148–150°C; IR (KBr, ν, cm^{-1}): 3491, 3323, 3189, 3056, 1624, 1591, 1539, 1508, 1474, 1272, 1219, 1103, 860, 815, 748, 669 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.78 (2H, s, NH_2), 7.56 (1H, s, ArH), 7.59–7.61 (2H, m, ArH), 7.62–7.64 (2H, m, ArH), 7.81 (1H, d, *J* = 2.0 Hz, ArH), 7.99 (2H, t, *J* = 2.4 Hz, ArH), 8.26 (2H, dd, *J* = 1.6 Hz, *J* = 8.8 Hz, ArH), 8.76 (1H, s, ArH); Anal. Calcd. for $C_{20}H_{13}Cl_2N_3$: C, 65.59; H, 3.58; N, 11.47. Found: C, 65.68; H, 3.50; N, 11.57. HRMS *m/z* calculated for $C_{20}H_{13}Cl_2N_3$ $[M + Na]^+$: 388.0384, found: 388.0399.

4-(3,4-Dichlorophenyl)-6-(naphthalen-2-yl)pyrimidin-2-amine (4h). M.p. 177–179°C; IR (KBr, ν, cm^{-1}): 3491, 3326, 3190, 3060, 1622, 1591, 1536, 1512, 1478, 1445, 1433, 1395, 1361, 1329, 1220, 1104, 829, 808, 788, 745, 669, 563 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.73 (2H, s, NH_2), 7.57 (1H, d, *J* = 1.6 Hz, ArH), 7.61 (3H, t, *J* = 6.0 Hz, ArH), 7.70 (1H, d, *J* = 8.4 Hz, ArH), 7.82 (1H, s, ArH), 8.00 (1H, t, *J* = 2.0 Hz, ArH), 8.06 (2H, d, *J* = 8.8 Hz, ArH), 8.26 (1H, dd, *J* = 1.6 Hz, *J* = 8.8 Hz, ArH), 8.76 (1H, s, ArH); Anal. Calcd. for $C_{20}H_{13}Cl_2N_3$: C, 65.59; H, 3.58; N, 11.47. Found: C, 65.72; H, 3.63; N, 11.38. HRMS *m/z* calculated for $C_{20}H_{13}Cl_2N_3$ $[M + Na]^+$: 388.0384, found: 388.0390.

4-(Naphthalen-1-yl)-6-phenylpyrimidin-2-amine (7a). M. p. 95–97°C; IR (KBr, ν, cm^{-1}): 3417, 3048, 1628, 1588, 1498, 1445, 1394, 1339, 1322, 1283, 1256, 1177, 1064, 1027, 881, 789, 774, 731, 712, 692, 668 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.80 (2H, s, NH_2), 7.28–7.34 (3H, m, ArH), 7.45 (1H, t, *J* = 8.0 Hz, ArH), 7.53 (1H, d, *J* = 7.6 Hz, ArH), 7.56–7.61 (3H, m, ArH), 7.67 (2H, d, *J* = 7.2 Hz, ArH), 7.94 (1H, d, *J* = 7.6 Hz, ArH), 8.00 (1H, d, *J* = 8.0 Hz, ArH), 8.05 (1H, d, *J* = 8.0 Hz, ArH); Anal. Calcd. for $C_{20}H_{15}N_3$: C, 80.78; H, 5.08; N, 14.13. Found: C, 80.61; H, 5.06; N, 14.20. HRMS *m/z* calculated for $C_{20}H_{15}N_3$ $[M + Na]^+$: 320.1164, found: 320.1178.

4-(Naphthalen-1-yl)-6-p-tolylpyrimidin-2-amine (7b). M.p. 141–142°C; IR (KBr, ν, cm^{-1}): 3322, 3170, 3043, 1649, 1613, 1561, 1535, 1458, 1397, 1351, 1234, 1213, 1185, 1115, 1032, 1018, 820, 797, 776, 752, 643, 594, 572 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.37 (3H, s, CH_3), 6.83 (2H, s, NH_2), 7.32 (3H, t, *J* = 8.0 Hz, ArH), 7.54–7.57 (2H, m, ArH), 7.62 (1H, t, *J* = 8.0 Hz, ArH), 7.72 (1H, d, *J* = 7.2 Hz, ArH), 8.01–8.09 (4H, m, ArH), 8.24 (1H, d, *J* = 7.2 Hz, ArH); Anal. Calcd. for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 81.22; H, 5.11; N, 13.31. HRMS *m/z* calculated for $C_{21}H_{17}N_3$ $[M + Na]^+$: 334.1320, found: 334.1333.

4-(4-Methoxyphenyl)-6-(naphthalen-1-yl)pyrimidin-2-amine (7c). M.p. 152–154°C; IR (KBr, ν, cm^{-1}): 3481, 3299, 3044, 3001, 2936, 2836, 1638, 1566, 1540, 1514, 1439, 1354, 1303, 1253, 1234, 1175, 1029, 822, 807, 781, 649, 581, 525 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.83 (3H, s, OCH_3), 6.78 (2H, s, NH_2), 7.06 (2H, d, *J* = 8.8 Hz, ArH), 7.32 (1H, s, ArH), 7.54–7.64 (3H, m, ArH), 7.71 (1H, d, *J* = 6.8 Hz, ArH), 8.03 (2H, t, *J* = 8.4 Hz, ArH), 8.13 (2H, d, *J* = 8.8 Hz, ArH), 8.23 (1H, d, *J* = 8.0 Hz, ArH); Anal. Calcd. for $C_{21}H_{17}N_3O$: C, 77.04; H, 5.23; N, 12.84. Found: C, 77.23; H, 5.19; N, 12.76. HRMS *m/z* calculated for $C_{21}H_{17}N_3O$ $[M + Na]^+$: 350.1269, found: 350.1277.

4-(2,4-Dimethylphenyl)-6-(naphthalen-1-yl)pyrimidin-2-amine (7d). M.p. 145–147°C; IR (KBr, ν, cm^{-1}): 3399, 3045, 3010, 2949, 1681, 1583, 1446, 1395, 1376, 1320, 1253, 1234, 1167, 1052, 1033, 776 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.21 (3H, s, CH_3), 2.27 (3H, s, CH_3), 6.73 (2H, s, NH_2), 7.10–7.13 (1H, m, ArH), 7.44–7.47 (1H, m, ArH), 7.56–7.63 (5H, m, ArH), 7.97 (2H, d, *J* = 8.0 Hz, ArH), 8.03 (2H, d, *J* = 8.0 Hz, ArH); Anal. Calcd. for $C_{22}H_{19}N_3$: C, 81.20; H, 5.89; N, 12.91. Found: C, 81.38; H, 5.83; N, 12.76. HRMS *m/z* calculated for $C_{22}H_{19}N_3$ $[M + Na]^+$: 348.1477, found: 348.1498.

4-(3-Chlorophenyl)-6-(naphthalen-1-yl)pyrimidin-2-amine (7e). M.p. 104–106°C; IR (KBr, ν, cm^{-1}): 3298, 3155, 3047, 1685, 1563, 1537, 1478, 1441, 1396, 1351, 1235, 1213, 1077, 878, 777, 719, 699, 627 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.95 (2H, s, NH_2), 7.63 (2H, d, *J* = 7.2 Hz, ArH), 7.69 (1H, d, *J* = 7.2 Hz, ArH), 7.75 (1H, d, *J* = 7.2 Hz, ArH), 7.89 (1H, d, *J* = 8.0 Hz, ArH), 7.93 (1H, d, *J* = 8.0 Hz, ArH), 8.02–8.05 (1H, m, ArH), 8.07 (1H, s, ArH), 8.15 (1H, d, *J* = 7.2 Hz, ArH), 8.18 (1H, s, ArH), 8.24–8.29 (2H, m, ArH); Anal. Calcd. for $C_{20}H_{14}ClN_3$: C, 72.40; H, 4.25; N, 12.66. Found: C, 72.59; H, 4.19; N, 12.58. HRMS *m/z* calculated for $C_{20}H_{14}ClN_3$ $[M + Na]^+$: 354.0774, found: 354.0790.

4-(2,4-Dichlorophenyl)-6-(naphthalen-1-yl)pyrimidin-2-amine (7f). M.p. 166–168°C; IR (KBr, ν, cm^{-1}): 3495, 3423, 3313, 3190, 1627, 1591, 1570, 1535, 1479, 1450, 1399, 1352, 1250, 1211, 1104, 862, 828, 799, 775 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 7.00 (2H, s, NH_2), 7.06 (1H, s, ArH), 7.57–7.64 (4H, m, ArH), 7.70–7.74 (2H, m, ArH), 7.78 (1H, d, *J* = 1.6 Hz, ArH), 8.04 (2H, dd, *J* = 5.2 Hz, *J* = 8.0 Hz, ArH), 8.28 (1H, t, *J* = 5.2 Hz, ArH); Anal. Calcd. for $C_{20}H_{13}Cl_2N_3$: C, 65.59; H, 3.58; N, 11.47. Found: C, 65.67; H, 4.03; N, 11.51. HRMS *m/z* calculated for $C_{20}H_{13}Cl_2N_3$ $[M + Na]^+$: 388.0384, found: 388.0397.

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REFERENCES AND NOTES

[1] Sayle, K. L.; Bentley, J. F.; Boyle, T.; Calvert, A. H.; Cheng, Y.; Curtin, N. J.; Endicott, J. A.; Golding, B. T.; Hardcastle, I. R.; Jewsbury, P. Bioorg Med Chem Lett 2003, 13, 3079.

[2] Arvanitis, A. G.; Gilligan, P. J.; Chorvat, R. J.; Cheeseman, R. S.; Christos, T. E.; Bakthavatchalam, R.; Beck, J. P.; Cocuzza, A. J.; Hobbs, F. W.; Wilde, R. G.; Arnold, C.; Chidester, D.; Curry, M.; He, L.; Hollis, A.; Klaczkiewicz, J.; Krenitsky, P. J.; Rescinito, J. P.; Scholfield, E.; Culp, S.; De Souza, E. B.; Fitzgerald, L.; Grigoriadis, D.; Tam, S. W.; Wong, Y. N.; Huang, S.; Shen, H. L. J Med Chem 1999, 42, 805.

[3] Savornin, B.; Madadi, N. E.; Delmas, F.; Gasquet, M.; Timon-David, P.; Vanelle, P.; Maldonado, J. J Pharm Pharmacol 1991, 43, 58.

[4] Balasankar, T.; Nagarajan, S. Heterocycl Commun 2004, 10, 465.

[5] Luo, G.; Chen, L.; Poindexter, G. S. Tetrahedron Lett 2002, 43, 5739.

[6] Calza, P.; Medana, C.; Baiocchi, C.; Pelizzetti, E. Appl Catal B: Environ 2004, 52, 267.

[7] (a) Cocco, M. T.; Congiu, C.; Liliu, V.; Onnis, V. Bioorg Med Chem 2006, 14, 366; (b) Gadhachanda, V. R.; Wu, B.; Wang, Z.; Kuhen, K. L.; Caldwell, J.; Zondler, H.; Walter, H.; Havenhand, H. M.; He, Y. Bioorg Med Chem Lett 2007, 17, 260.

[8] Baskaran, S.; Hanan, E.; Byun, D.; Shen, W. Tetrahedron Lett 2004, 45, 2107.

[9] Akyuz, S.; Akyuz, T. J Mol Struct 2005, 277, 744.

[10] Akyuz, S. J Supramol Chem 2002, 2, 401.

[11] (a) El-Hashash, M. A.; Mahhmoud, M. R.; Madboli, S. A. Indian J Chem 1993, 32, 449; (b) Rashinkar, G. S.; Pore, S. B.; Mote, K. B.; Salunkhe, R. S. Indian J Chem 2009, 48, 606.

[12] El-Hashash, M. A.; Mahhmoud, M. R.; Madboli, S. A. Indian J Chem 1993, 32, 449.

[13] Goswami, S.; Jana, S.; Dey, S.; Adak, A. K. Aust J Chem 2007, 60, 120.

[14] Sharma, V.; Mclaughlin, M. L. J Comb Chem 2010, 12, 327.

[15] Ingarsal, N.; Saravanan, G.; Amutha, P.; Nagarajan, S. Eur J Chem 2007, 42, 517.

[16] Kanagarajan, V.; Thanusu, J.; Gopalakrishnan, M. Eur J Med Chem 2010, 45, 1583.

[17] Nguyen, T. B.; Martel, A.; Dhal, R.; Dujardin, G. J Org Chem 2008, 73, 2621.

[18] Chandra, M.; Volla, R.; Vogel, P. Org Lett 2009, 11, 1701.

[19] Yan, B.; Lin, Y. H. Org Lett 2007, 9, 4323.

[20] Shi, D. Q.; Dou, G. L. Synth Commun 2008, 38, 3329.