An Efficient and Convenient Multicomponent Reaction for the Synthesis of 2-Methyl-4,6-Diarylpyrimidine Under Solvent-Free Conditions

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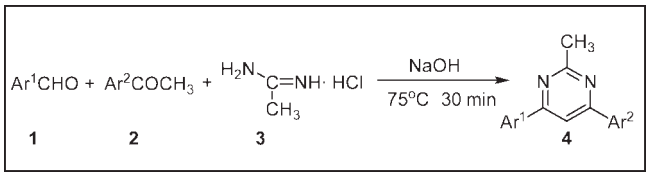

An efficient and convenient method for the preparation of 2-methyl-4,6-diarylpyrimidine derivatives by the multicomponent reactions of aromatic aldehydes, aromatic ketones, and acetamidine hydrochloride in the presence of sodium hydroxide under solvent-free conditions was reported. This method has the advantages of excellent yields, mild reaction conditions, easy workup, and environmentally friendly procedure.

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INTRODUCTION

In recent years, multicomponent reactions (MCRs) have emerged as a powerful strategy to construct useful molecules from simple starting materials [1]. Molecules synthesized by this method continue attracting the attention of medicinal and synthetic chemists [2]. The pyrimidines and their derivatives, as the important heterocyclic compounds, are an integral part of various natural products [3] and serve as a building block for various pharmaceuticals and biopolymers. It also has very good coordinating ability similar to pyridyl ligands in supramolecular metallogrid-like architecture [4]. In addition, pyrimidines are pharmacologically active and display anticonvulsant [5], anti-inflammatory [6], antibacterial [7], and antimycotic [8] activities. Therefore, synthesis of pyrimidine derivatives is always an important field for chemists. Some MCRs for the synthesis of pyrimidines or their derivatives have been reported [9].

Solvent-free organic synthesis is a well-established method for the synthesis of organic molecules [10] because it has some advantages, such as high efficiency and selectivity, easy separation and purification, and mild reaction conditions. As part of our continued interest in the development of highly expedient methods for the synthesis of organic compounds [11], herein, we would like to report a MCR for the synthesis of 2-methyl-4,6-diarylpyrimidine derivatives under solvent-free conditions.

RESULTS AND DISCUSSION

The first step of this synthetic approach consists of finding out the optimized reaction conditions. The optimization was begun by studying the effect of various solvents and solvent-free conditions on the model reaction of 4-chlorobenzaldehyde, acetophenone, and acetamidine hydrochloride in the presence of some different catalysts. As the data in Table 1 indicated, the results of reaction were quite different. When the reaction was carried out in solvent conditions using piperidine ($C_5H_{11}N$), triethylamine (Et_3N), and NaOH as catalyst, the results of reactions were not satisfying. We probably thought that acetamidine hydrochloride is the inorganic salt and does not easily dissolve in the organic solvents, so the reactions do not put out well. Then, the reaction was carried out under solvent-free conditions at 75°C. When piperidine ($C_5H_{11}N$) or triethylamine (Et_3N) was used as catalyst, the reaction was unsatisfactory. When the NaOH was chosen as catalyst, the reaction could be carried out smoothly, and the 4-(4-chlorophenyl)-2-methyl-6-phenylpyrimidine **4a** could be obtained with high yields (96%). We also investigated the reaction outcome using different amounts of NaOH. By increasing the quantity of NaOH from 0.05 to 0.3 g, the reaction gave different outcomes, resulting in the isolation of **4a** in about 85, 96, 92, and 90% yields, respectively. Higher loading of the catalyst did not improve the yields of the reaction. Perhaps, more NaOH could turn the reagents into solid more quickly, which hindered the reaction from completion.

With this optimum condition in hand, we synthesized 2-methyl-4,6-diarylpyrimidine derivatives under solvent-free conditions. The procedure of reaction was very facile: the mixture of aromatic aldehydes, aromatic ketones, and acetamidine hydrochloride was put into a flask, in

Table 1

Synthesis of **4a** under different conditions in the presence of different catalysts.[a]

Entry	Solvent	Amount	Yields[b] (%)
1	MeOH	$C_5H_{11}N$ (0.05 mL)	Trace
2	MeOH	Et_3N (0.05 mL)	Trace
3	MeOH	NaOH (0.1 g)	<5
4	EtOH	$C_5H_{11}N$ (0.05 mL)	Trace
5	EtOH	Et_3N (0.05 mL)	Trace
6	EtOH	NaOH (0.1 g)	<5
7	CH_3CN	$C_5H_{11}N$ (0.05 mL)	0
8	CH_3CN	Et_3N (0.05 mL)	0
9	CH_3CN	NaOH (0.1 g)	0
10	DMF	$C_5H_{11}N$ (0.05 mL)	0
11	DMF	Et_3N (0.05 mL)	0
12	DMF	NaOH (0.1 g)	0
13	Neat	$C_5H_{11}N$ (0.05 mL)	Trace
14	Neat	Et_3N (0.05 mL)	Trace
15	Neat	NaOH (0.05 g)	85
16	Neat	NaOH (0.1 g)	96
17	Neat	NaOH (0.2 g)	92
18	Neat	NaOH (0.3 g)	90

[a] Reagents and conditions: 4-chlorobenzaldehyde, **1** (2 mmol), acetophenone aldehydes **2** (2 mmol), acetamidine hydrochloride **3** (2 mmol).
[b] Isolated yields.

the presence of 0.1 g NaOH as catalyst, and let them at 75°C under solvent-free conditions, a series of 2-methyl-4,6-diarylpyrimidine derivatives could be prepared with high yield. The results of the reactions are summarized in Table 2.

The reaction was efficiently completed under solvent-free conditions. From Table 2, we could find that the aldehydes or ketones bearing either electron-withdrawing or electron-donating groups perform well in this reaction. Therefore, we concluded that the electronic nature of the substituents has no significant effect on this reaction. The structure of each product **4a–w** was established on the basis of spectroscopic data, particularly ^{1}H NMR analysis and HRMS spectra.

In conclusion, we have successfully developed an efficient and facile method to prepare a variety of 2-methyl-4,6-diarylpyrimidine derivatives *via* the MCRs of different aromatic aldehydes, aromatic ketones, and acetamidine hydrochloride under solvent-free conditions. In this reaction, we found that NaOH was an excellent catalyst, because the reaction could be efficiently completed when it existed, and that do not consider the quality of substituent groups. Because no toxic organic solvent was used, the simplicity of the reaction procedure coupled with excellent yields, making this method one of the most efficient methods for the synthesis of these kinds of heterocyclic compounds.

EXPERIMENTAL

Melting points were determined on XT-5 microscopic melting-point apparatus and were uncorrected. IR spectra were recorded on a FT Bruker Tensor 27 spectrometer. ^{1}H NMR spectra were obtained from solution in DMSO-d_6 with Me_4Si as an 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 2-methyl-4,6-diarylpyrimidine derivatives. The mixture of aromatic aldehydes **1** (2 mmol), aromatic ketones **2** (2 mmol), acetamidine hydrochloride **3** (2 mmol), and NaOH (0.1 g) was put in a reaction flask and let at 75°C for about 30 min. After completing the reaction, the reaction mixture was poured into water (0.5% HCl) and then washed with water thoroughly. The product was filtered, dried, and recrystallized from 95% ethanol.

4-(4-Chlorophenyl)-2-methyl-6-phenylpyrimidine (4a). This compound was obtained as white crystals, mp 95–96°C; IR: (KBr, ν, cm^{-1}): 3054, 2842, 1585, 1570, 1533, 1441, 1393, 1234, 1183, 1159, 1119, 1089, 1031, 1013, 1001, 990, 907, 867, 834, 779, 753, 713, 686, 642, 602, 582 cm^{-1}; ^{1}H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.73 (3H, s, CH_3), 7.56–7.58 (3H, m, ArH), 7.62 (2H, d, J = 8.0 Hz, ArH), 8.33–8.36 (3H, m, ArH), 8.40 (2H, J = 8.0 Hz, ArH). *Anal*. Calcd for $C_{17}H_{13}ClN_2$: C, 72.73; H, 4.67; N, 9.98. Found: C, 72.60; H, 4.70; N, 9.94. HRMS *m/z* calculated for $C_{17}H_{13}ClN_2$ [M + H]: 281.0846; found: 281.0845.

4-(4-Fluorophenyl)-2-methyl-6-phenylpyrimidine (4b). This compound was obtained as white crystals, mp 100–102°C, Lit. [12] 108–109°C; IR: (KBr, ν, cm^{-1}): 3042, 2932, 1602, 1578, 1534, 1509, 1417, 1394, 1369, 1297, 1227, 1163, 1099, 1074,

Table 2

Synthesis of 2-methyl-4,6-diarylpyrimidine derivatives under solvent-free conditions.

Entry	Ar^1	Ar^2	Product	Yields
1	4-ClC_6H_4	C_6H_5	**4a**	96
2	4-FC_6H_4	C_6H_5	**4b**	95
3	4-$CH_3C_6H_4$	C_6H_5	**4c**	89
4	4-$CH_3OC_6H_4$	C_6H_5	**4d**	90
5	4-FC_6H_4	4-$CH_3OC_6H_4$	**4e**	92
6	4-$CH_3C_6H_4$	4-$CH_3OC_6H_4$	**4f**	90
7	4-$CH_3OC_6H_4$	4-$CH_3OC_6H_4$	**4g**	84
8	3-ClC_6H_4	4-$CH_3OC_6H_4$	**4h**	87
9	3,4-$(CH_3)_2C_6H_3$	4-$CH_3OC_6H_4$	**4i**	90
10	3,4-$(CH_3O)_2C_6H_3$	4-$CH_3OC_6H_4$	**4j**	80
11	4-FC_6H_4	3-ClC_6H_4	**4k**	92
12	4-$CH_3C_6H_4$	3-ClC_6H_4	**4l**	88
13	4-FC_6H_4	4-$CH_3C_6H_4$	**4m**	87
14	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	**4n**	86
15	4-FC_6H_4	4-ClC_6H_4	**4o**	89
16	4-ClC_6H_4	4-ClC_6H_4	**4p**	90
17	4-$CH_3C_6H_4$	4-ClC_6H_4	**4q**	92
18	4-$CH_3OC_6H_4$	4-ClC_6H_4	**4r**	90
19	3,4-$(CH_3)_2C_6H_3$	4-ClC_6H_4	**4s**	80
20	3,4-$(CH_3O)_2C_6H_3$	4-ClC_6H_4	**4t**	84
21	3-ClC_6H_4	4-ClC_6H_4	**4u**	94
22	3,4-$Cl_2C_6H_3$	4-ClC_6H_4	**4v**	88
23	4-BrC_6H_4	4-ClC_6H_4	**4w**	83

1012, 841, 777, 756, 720, 690, 648 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.75 (3H, s, CH_3), 7.40 (2H, d, J = 8.8 Hz, J = 8.8 Hz, ArH), 7.57 (3H, t, J =3.6 Hz, J = 2.8 Hz, ArH), 8.33–8.36 (2H, m, ArH), 8.41–8.45 (3H, m, ArH). *Anal*. Calcd for $C_{17}H_{13}FN_2$: C, 77.25; H, 4.96; N, 10.60. Found: C, 77.40; H, 4.94; N, 10.56. HRMS *m/z* calculated for $C_{17}H_{13}FN_2$ [M + H]: 265.1141; found: 265.1146.

2-Methyl-4-phenyl-6-*p*-tolylpyrimidine (4c). This compound was obtained as white crystals, mp 99–100°C; IR: (KBr, ν, cm^{-1}): 3034, 2920, 1572, 1528, 1448, 1390, 1367, 1344, 1305, 1235, 1186, 1122, 1077, 1021, 989, 904, 875, 834, 818, 782, 759, 717, 698, 648 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.40 (3H, s, CH_3), 2.74 (3H, s, CH_3), 7.37 (2H, d, J = 8.0 Hz, ArH), 7.56 (3H, t, J = 3.6 Hz, J = 3.6 Hz, ArH), 8.25 (2H, d, J = 8.0 Hz, ArH), 8.32–8.34 (2H, m, ArH), 8.36 (1H, s, ArH). *Anal*. Calcd for $C_{18}H_{16}N_2$: C, 83.04; H, 6.19; N, 10.76. Found: C, 83.20; H, 6.17; N, 10.72. HRMS *m/z* calculated for $C_{18}H_{16}N_2$ [M + H]: 261.1392; found: 261.1390.

4-(4-Methoxyphenyl)-2-methyl-6-phenylpyrimidine (4d). This compound was obtained as white crystals, mp 94–96°C, Lit. [13] 103–104°C; IR: (KBr, ν, cm^{-1}): 2965, 2842, 1602, 1573, 1441, 1368, 1295, 1255, 1185, 1170, 1030, 987, 874, 829, 783, 763, 727, 698, 589 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.72 (3H, s, CH_3), 3.85 (3H, s, OCH_3), 7.10 (2H, d, J = 8.8 Hz, ArH), 7.56 (3H, t, J = 2.8 Hz, J = 3.2 Hz, ArH), 8.32 (5H, d, J = 6.4 Hz, ArH). *Anal*. Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14. Found: C, 78.19; H, 5.86; N, 10.18. HRMS *m/z* calculated for $C_{18}H_{16}N_2O$ [M + H]: 277.1341; found: 277.1338.

4-(4-Fluorophenyl)-6-(4-methoxyphenyl)-2-methylpyrimidine (4e). This compound was obtained as white crystals, mp 107–109°C; IR: (KBr, ν, cm^{-1}): 3041, 3005, 2972, 2938, 2937, 1602, 1509, 1414, 1371, 1299, 1259, 1173, 1096, 1030, 846, 822, 764 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.71 (3H, s, CH_3), 3.85 (3H, s, OCH_3), 7.10 (2H, d, J = 8.8 Hz, ArH), 7.39 (2H, t, J = 8.8 Hz, J = 8.8 Hz, ArH), 8.32 (3H, d, J = 6.8 Hz, ArH), 8.38–8.42 (2H, dd, J = 5.6 Hz, J = 5.6 Hz, ArH). *Anal*. Calcd for $C_{18}H_{15}FN_2O$: C, 73.45; H, 5.14; N, 9.52. Found: C, 73.51; H, 5.15; N, 9.50. HRMS *m/z* calculated for $C_{18}H_{15}FN_2O$ [M + H]: 295.1247; found: 295.1248.

4-(4-Methoxyphenyl)-2-methyl-6-*p*-tolylpyrimidine (4f). This compound was obtained as white crystals, mp 119–120°C; IR: (KBr, ν, cm^{-1}): 3014, 2968, 2971, 2840, 1609, 1585, 1525, 1456, 1442, 1410, 1371, 1340, 1303, 1256, 1172, 1113, 1024, 827, 776, 759, 574 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.40 (3H, s, CH_3), 2.71 (3H, s, CH_3), 3.86 (3H, s, OCH_3), 7.09 (2H, d, J = 8.8 Hz, ArH), 7.36 (2H, d, J = 8.0, Hz, ArH), 8.23 (2H, d, J = 8.0 Hz, ArH), 8.28 (1H, s, ArH), 8.32 (2H, d, J = 8.4 Hz, ArH). *Anal*. Calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.70; H, 6.27; N, 9.62. HRMS *m/z* calculated for $C_{19}H_{18}N_2O$ [M + H]: 291.1497; found: 291.1499.

4,6-Bis(4-methoxyphenyl)-2-methylpyrimidine (4g). This compound was obtained as white crystals, mp 159–160°C; IR: (KBr, ν, cm^{-1}): 3006, 2969, 2939, 2839, 1606, 1525, 1455, 1416, 1374, 1302, 1255, 1171, 1113, 1026, 830, 777, 636, 575 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.69 (3H, s, CH_3), 3.85 (6H, s, 2 × OCH_3), 7.09 (4H, d, J = 8.8 Hz, ArH), 8.25 (1H, s, ArH), 8.32 (4H, d, J = 8.8 Hz, ArH). *Anal*. Calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14. Found: C, 74.62; H, 5.89; N, 9.18. HRMS *m/z* calculated for $C_{19}H_{18}N_2O_2$ [M + H]: 307.1447; found: 307.1446.

4-(3-Chlorophenyl)-6-(4-methoxyphenyl)-2-methylpyrimidine (4h). This compound was obtained as white crystals, mp 85–86°C; IR: (KBr, ν, cm^{-1}): 3066, 2974, 2938, 2842, 1608, 1572, 1511, 1462, 1420, 1364, 1292, 1240, 1192, 1174, 1027, 831, 802, 691, 590 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.71 (3H, s, CH_3), 3.86 (3H, s, OCH_3), 7.10 (2H, d, J = 8.8 Hz, ArH), 7.57–7.63 (2H, m, ArH), 8.30 (1H, d, J = 7.2 Hz, ArH), 8.34 (2H, d, J = 8.8 Hz, ArH), 8.39 (2H, s, ArH). *Anal*. Calcd for $C_{18}H_{15}ClN_2O$: C, 69.57; H, 4.86; N, 9.01. Found: C, 69.66; H, 4.84; N, 9.05. HRMS *m/z* calculated for $C_{18}H_{15}ClN_2O$ [M + H]: 311.0951; found: 311.0951.

4-(3,4-Dimethylphenyl)-6-(4-methoxyphenyl)-2-methylpyrimidine (4i). This compound was obtained as white crystals, mp 92–93°C; IR: (KBr, ν, cm^{-1}): 3010, 2966, 2938, 2919, 2841, 1610, 1574, 1455, 1410, 1360, 1339, 1303, 1243, 1171, 1113, 1025, 874, 828, 805, 761, 578 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.30 (3H, s, CH_3), 2.34 (3H, s, CH_3), 2.71 (3H, s, CH_3) 3.85 (3H, s, OCH_3), 7.09 (2H, d, J = 9.2 Hz, ArH), 7.30 (1H, d, J = 7.6 Hz, ArH), 8.05 (1H, d, J = 8.0 Hz, ArH), 8.20 (1H, s, ArH), 8.27 (1H, s, ArH), 8.31 (2H, d, J = 8.8 Hz, ArH). *Anal*. Calcd for $C_{20}H_{20}N_2O$: C, 78.92; H, 6.62; N, 9.20. Found: C, 78.78; H, 6.65; N, 9.16. HRMS *m/z* calculated for $C_{20}H_{20}N_2O$ [M + H]: 305.1654; found: 305.1654.

4-(3,4-Dimethoxyphenyl)-6-(4-methoxyphenyl)-2-methylpyrimidine (4j). This compound was obtained as white crystals, mp 116–117°C; IR: (KBr, ν, cm^{-1}): 3086, 2997, 2960, 2931, 2833, 1574, 1510, 1439, 1362, 1345, 1293, 1251, 1172, 1117, 1095, 1020, 883, 832, 803, 765, 616, 575 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.70 (3H, s, CH_3), 3.85 (6H, s, 2 × OCH_3), 3.90 (3H, s, CH_3), 7.09–7.12 (3H, dd, J = 4.4 Hz, J = 4.4 Hz, ArH), 7.86 (1H, d, J = 2.0 Hz, ArH), 7.96 (1H, dd, J = 2.0 Hz, J = 2.0 Hz, ArH), 8.26 (1H, s, ArH), 8.32 (2H, d, J = 8.8 Hz, ArH). *Anal*. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.55; H, 5.97; N, 8.29. HRMS *m/z* calculated for $C_{20}H_{20}N_2O_3$ [M + H]: 337.1552; found: 337.1555.

4-(3-Chlorophenyl)-6-(4-fluorophenyl)-2-methylpyrimidine (4k). This compound was obtained as white crystals, mp 105–106°C; IR: (KBr, ν, cm^{-1}): 3020, 2925, 1582, 1537, 1505, 1365, 1296, 1221, 1158, 1126, 1096, 1013, 990, 869, 854, 832, 791, 764, 715, 688, 653 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.71 (3H, s, CH_3), 7.37 (2H, t, J = 8.8 Hz, J = 8.8 Hz, ArH), 7.58 (2H, t, J = 8.8 Hz, J = 8.8 Hz, ArH), 8.27 (1H, d, J = 7.2 Hz, ArH), 8.37–8.41 (4H, m, ArH). *Anal*. Calcd for $C_{17}H_{12}ClFN_2$: C, 68.35; H, 4.05; N, 9.38. Found: C, 68.45; H, 4.07; N, 9.34. HRMS *m/z* calculated for $C_{17}H_{12}ClFN_2$ [M + H]: 299.0751; found: 299.0751.

4-(3-Chlorophenyl)-2-methyl-6-*p*-tolylpyrimidine (4l). This compound was obtained as white crystals, mp 76–77°C; IR: (KBr, ν, cm^{-1}): 3025, 2930, 1612, 1569, 1511, 1364, 1238, 1181, 1126, 1068, 989, 834, 815, 799, 761, 714, 690, 655, 646 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.40 (3H, s, CH_3), 2.74 (3H, s, CH_3), 7.37 (2H, d, J = 8.0 Hz, ArH), 7.57–7.64 (2H, m, ArH), 8.27 (2H, d, J = 8.4 Hz, ArH), 8.31 (1H, d, J = 7.6 Hz, ArH), 8.41 (2H, d, J = 9.2 Hz, ArH). *Anal*. Calcd for $C_{18}H_{15}ClN_2$: C, 73.34; H, 5.13; N, 9.50. Found: C, 73.45; H, 5.15; N, 9.47. HRMS *m/z* calculated for $C_{18}H_{15}ClN_2$ [M + H]: 295.1002; found: 295.1004.

4-(4-Fluorophenyl)-2-methyl-6-*p*-tolylpyrimidine (4m). This compound was obtained as white crystals, mp 95–96°C; IR: (KBr, ν, cm^{-1}): 3020, 2924, 1591, 1584, 1536, 1507, 1445, 1411, 1362, 1226, 1162, 1123, 1097, 1013, 847, 826, 814, 760, 642 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.39 (3H, s, CH_3), 2.72 (3H, s, CH_3), 735–7.41 (4H, m, ArH), 8.24 (2H, d, $J = 8.0$ Hz, ArH), 8.35 (1H, s, ArH), 8.38–8.42 (2H, dd, $J = 5.6$ Hz, $J = 5.6$ Hz, ArH).

Anal. Calcd for $C_{18}H_{15}FN_2$: C, 77.68; H, 5.43; N, 10.07. Found: C, 77.57; H, 5.40; N, 10.11. HRMS *m/z* calculated for $C_{18}H_{15}FN_2$ [M + H]: 279.1298; found: 279.1296.

2-Methyl-4,6-dip-tolylpyrimidine (4n). This compound was obtained as white crystals, mp 130–131°C, Lit. [14] 137–139°C; IR: (KBr, ν, cm^{-1}): 3026, 2920, 1582, 1508, 1444, 1408, 1365, 1240, 1208, 1122, 1017, 826, 813, 758, 600 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.40 (6H, s, 2 × CH_3), 2.73 (3H, s, CH_3), 7.37 (4H, d, $J = 8.0$ Hz, ArH), 8.24 (4H, d, $J = 8.0$ Hz, ArH), 8.32 (1H, s, ArH). *Anal*. Calcd for $C_{19}H_{18}N_2$: C, 83.18; H, 6.61; N, 10.21. Found: C, 83.27; H, 6.59; N, 10.24. HRMS *m/z* calculated for $C_{19}H_{18}N_2$ [M + H]: 275.1548; found: 275.1549.

4-(4-Chlorophenyl)-6-(4-fluorophenyl)-2-methylpyrimidine (4o). This compound was obtained as white crystals, mp 148–149°C; IR: (KBr, ν, cm^{-1}): 3044, 2972, 2950, 2851, 1600, 1548, 1509, 1491, 1415, 1391, 1364, 1229, 1162, 1088, 1012, 829, 762, 590 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.74 (3H, s, CH_3), 7.40 (2H, t, $J = 8.8$ Hz, $J = 8.8$ Hz, ArH), 7.63 (2H, d, $J = 8.4$ Hz, ArH), 8.37 (1H, s, ArH), 8.39–8.45 (4H, m, ArH). *Anal*. Calcd for $C_{17}H_{12}ClFN_2$: C, 68.35; H, 4.05; N, 9.38. Found: C, 68.21; H, 4.07; N, 9.35. HRMS *m/z* calculated for $C_{17}H_{12}ClFN_2$ [M + H]: 299.0751; found: 299.0740.

4,6-Bis(4-chlorophenyl)-2-methylpyrimidine (4p). This compound was obtained as white crystals, mp 144–146°C; IR: (KBr, ν, cm^{-1}): 3057, 2978, 2955, 2859, 1565, 1529, 1488, 1365, 1291, 1232, 1172, 1120, 1091, 1012, 827, 804, 763, 726 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.72 (3H, s, CH_3), 7.61 (4H, d, $J = 8.4$ Hz ArH), 8.35 (4H, d, $J = 8.4$ Hz, ArH), 8.42 (1H, s, ArH). *Anal*. Calcd for $C_{17}H_{12}Cl_2N_2$: C, 64.78; H, 3.84; N, 8.89. Found: C, 64.65; H, 3.82; N, 8.85. HRMS *m/z* calculated for $C_{17}H_{12}Cl_2N_2$ [M + H]: 315.0456; found: 315.0464.

4-(4-Chlorophenyl)-2-methyl-6-*p*-tolylpyrimidine (4q). This compound was obtained as white crystals, mp 120–121°C; IR: (KBr, ν, cm^{-1}): 3025, 2950, 2922, 2830, 1580, 1509, 1491, 1407, 1237, 1212, 1188, 1121, 1099, 1089, 1011, 825, 813, 778, 758, 708 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.40 (3H, s, CH_3), 2.73 (3H, s, CH_3), 7.37 (2H, d, $J = 8.4$ Hz, ArH), 7.62 (2H, d, $J = 8.4$ Hz, ArH), 8.25 (2H, d, $J = 8.4$ Hz, ArH), 8.37 (3H, d, $J = 8.8$ Hz, ArH).

Anal. Calcd for $C_{18}H_{15}ClN_2$: C, 73.34; H, 5.13; N, 9.50. Found: C, 73.46; H, 5.15; N, 9.47. HRMS *m/z* calculated for $C_{18}H_{15}ClN_2$ [M + H]: 295.1002; found: 295.1009.

4-(4-Chlorophenyl)-6-(4-methoxyphenyl)-2-methylpyrimidine (4r). This compound was obtained as white crystals, mp 120–121°C; IR: (KBr, ν, cm^{-1}): 3055, 2974, 2935, 2834, 1610, 1586, 1530, 1513, 1491, 1454, 1412, 1368, 1288, 1257, 1235, 1169, 1119, 1097, 1024, 1010, 819, 779, 761, 594, 575 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.71 (3H, s, CH_3), 3.85 (3H, s, OCH_3), 7.09 (2H, d, $J = 8.4$ Hz, ArH), 7.61 (2H, d, $J = 8.4$ Hz, ArH), 8.31 (1H, s, ArH), 8.33–8.37 (4H, t, $J = 7.2$ Hz, $J = 7.2$ Hz, ArH).

Anal. Calcd for $C_{18}H_{15}ClN_2O$: C, 69.57; H, 4.86; N, 9.01. Found: C, 69.45; H, 4.84; N, 9.04. HRMS *m/z* calculated for $C_{18}H_{15}ClN_2O$ [M + H]: 311.0951; found: 311.0948.

4-(4-Chlorophenyl)-6-(3,4-dimethylphenyl)-2-methylpyrimidine (4s). This compound was obtained as white crystals, mp 96–97°C; IR: (KBr, ν, cm^{-1}): 2967, 2942, 2920, 2855, 1581, 1530, 1490, 1443, 1407, 1369, 1340, 1283, 1244, 1132, 1104, 1086, 1023, 1011, 873, 832, 788, 763, 583 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.29 (3H, s, CH_3), 2.33 (3H, s, CH_3), 2.71 (3H, s, CH_3), 7.30 (1H, d, $J = 8.0$ Hz, ArH), 7.61(2H, d, $J = 8.8$ Hz, ArH), 8.06 (1H, d, $J = 8.0$ Hz, ArH), 8.12 (1H, s, ArH), 8.34 (2H, d, $J = 2.4$ Hz, ArH), 8.36 (1H, s, ArH).

Anal. Calcd for $C_{19}H_{17}ClN_2$: C, 73.90; H, 5.55; N, 9.07. Found: C, 73.81; H, 5.57; N, 9.11. HRMS *m/z* calculated for $C_{19}H_{17}ClN_2$ [M + H]: 309.1159; found: 309.1159.

4-(4-Chlorophenyl)-6-(3,4-dimethoxyphenyl)-2-methylpyrimidine (4t). This compound was obtained as white crystals, mp 135–137°C; IR: (KBr, ν, cm^{-1}): 3002, 2973, 2959, 2934, 2831, 1584, 1489, 1440, 1410, 1324, 1268, 1216, 1178, 1134, 1096, 1025, 843, 822, 808, 785, 767, 622, 612, 580 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.72 (3H, s, CH_3), 3.85 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 7.11(1H, d, $J = 8.4$ Hz, ArH), 7.62 (2H, d, $J = 8.8$ Hz, ArH), 7.87 (1H, d, $J = 2.0$ Hz, ArH), 7.97–7.99 (1H, dd, $J = 2.0$ Hz, J =2.0 Hz, ArH), 8.36 (2H, s, ArH), 8.38 (1H, s, ArH). *Anal*. Calcd for $C_{19}H_{17}Cl_2N_2O_2$: C, 66.96; H, 5.03; N, 8.22. Found: C, 66.82; H, 5.05; N, 8.18. HRMS *m/z* calculated for $C_{19}H_{17}ClN_2O_2$ [M + H]: 341.1057; found: 341.1057.

4-(3-Chlorophenyl)-6-(4-chlorophenyl)-2-methylpyrimidine (4u). This compound was obtained as white crystals, mp 111–113°C; IR: (KBr, ν, cm^{-1}): 3006, 2977, 2963, 2835, 1580, 1491, 1408, 1366, 1294, 1266, 1235, 1178, 1127, 1090, 1013, 845, 833, 812, 793, 766, 734, 695, 689, 654, 642 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.73 (3H, s, CH_3), 7.56–7.62 (4H, m, ArH) 8.30 (1H, d, $J = 7.2$ Hz, ArH), 8.37 (3H, d, $J = 8.8$ Hz, ArH), 8.47 (1H, s, ArH). *Anal*. Calcd for $C_{17}H_{12}Cl_2N_2$: C, 64.78; H, 3.84; N, 8.89. Found: C, 64.59; H, 3.86; N, 9.92. HRMS *m/z* calculated for $C_{17}H_{12}Cl_2N_2$ [M + H]: 315.0456; found: 315.0451.

4-(4-Chlorophenyl)-6-(3,4-dichlorophenyl)-2-methylpyrimidine (4v). This compound was obtained as white crystals, mp 178–179°C; IR: (KBr, ν, cm^{-1}): 3021, 2992, 2978, 2850, 1595, 1575, 1491, 1472, 1405, 1387, 1339, 1398, 1233, 1139, 1088, 1026, 1011, 866, 850, 824, 765, 752, 699, 675 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.73 (3H, s, CH_3), 7.62 (2H, d, $J = 8.4$ Hz, ArH), 7.81 (1H, d, $J = 8.4$ Hz, ArH), 8.32 (1H, d, $J = 8.4$ Hz, ArH), 8.37 (2H, d, $J = 8.4$ Hz, ArH), 8.50 (1H, s, ArH), 8.59 (1H, s, ArH). *Anal*. Calcd for $C_{17}H_{11}Cl_3N_2$: C, 58.40; H, 3.17; N, 8.01. Found: C, 58.56; H, 3.19; N, 8.04. HRMS *m/z* calculated for $C_{17}H_{11}Cl_3N_2$ [M + H]: 349.0066; found: 349.0053.

4-(4-Bromophenyl)-6-(4-chlorophenyl)-2-methylpyrimidine (4w). This compound was obtained as white crystals, mp 142–144°C; IR: (KBr, ν, cm^{-1}): 2968, 2943, 2921, 2856, 1582, 1526, 1485, 1439, 1407, 1388, 1365, 1241, 1292, 1232, 1097, 1088, 1069, 1010, 825, 805, 762 cm^{-1}; ^1H NMR: (400 Hz, DMSO-d_6), (δ, ppm): 2.72 (3H, s, CH_3), 7.60 (2H, d, $J = 8.8$ Hz, ArH), 7.74 (2H, d, $J = 8.8$ Hz, ArH), 8.27 (2H, d, $J = 8.4$ Hz, ArH), 8.34 (2H, d, $J = 8.4$ Hz, ArH), 8.42 (1H, s, ArH). *Anal*. Calcd for $C_{17}H_{12}BrClN_2$: C, 56.77; H, 3.36; N,

7.79. Found: C, 56.65; H, 3.34; N, 7.75. HRMS *m/z* calculated for $C_{17}H_{12}ClBrN_2$ [M + H]: 358.9951; found: 358.9951.

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