SYNTHESIS OF 4-ARYL AND UNSYMMETRICAL 4,6-DIARYLPYRIMIDINES BY THE SUZUKI-MIYAUERA CROSS-COUPLING REACTION

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To Kiyoshi Tomioka, an individualistic organic chemist who has enriched our field: Koki (呉) 

Abstract – A two-step procedure for the synthesis of 4-arylpymridines from inexpensive 4,6-dichloropyrimidine via a Suzuki-Miyaura/hydrodechlorination reaction sequence is described. The reaction resulted in the predominant formation of mono-arylated product. The cross-coupling of 4-chloro-6-substituted pyrimidines with various aryl/heteroarylboronic acids also furnished 4,6-disubstituted pyrimidines in acceptable yields.

INTRODUCTION

Pyrimidines represent a long-standing class of heterocycles with significance in areas of biologically active compounds (Figure 1),1 e.g., imatinib (1), fluacrypyrim, rosuvastatin (2), AZD5438 (3),1d CDK9/CycT1 inhibitor (4),2 and buparlisib (5),3 materials with nonlinear optical (NLO)4b and photoluminescent (6)4 properties, and ligands for the molecular recognition of metal cations (7)5 and proteins.6
The traditional methods for the synthesis of arylated pyrimidines by de novo approaches\(^5,7\) have been superseded by the discovery and extensive development of transition metal catalyzed cross-coupling\(^8a,9\) and C-H activation/arylation reactions,\(^8\) which take advantage of the commercial availability of relatively inexpensive chlorinated pyrimidines.\(^10\) In these reactions, the \(\pi\)-electron deficiency of heteroaryl chlorides in general, and of pyrimidine chlorides in particular, facilitates oxidative addition to the C-Cl bond without the use of specialized ligands.\(^11\) Of the available cross-coupling Name Reactions, the Suzuki-Miyaura reaction\(^8a,9\) has witnessed the broadest utility. While the Suzuki-Miyaura reaction on polyhalogenated pyrimidines such as 2,4,5,6-tetrachloropyrimidine,\(^12\) 2,4,6-trichloropyrimidine,\(^9b,11c,13\) 2,4-dichloropyrimidines,\(^14\) 2,5-dihalopyrimidines\(^15\) and 4,6-dihalopyrimidines\(^16\) with arylboronic acids coupling partners are known, bromo- and iodo-pyrimidines have received scant attention possibly due to their expense. Furthermore, selective mono-arylation of dihalopyrimidines has been studied: 2-chloro-4-bromopyrimidine undergoes the expected faster reaction at the C-Br bond but results in significant amounts of unreacted starting material.\(^15c\) The 2,4-dibromo and 2,4-diiodo derivatives lead to equal mixtures of mono- and di-arylated products,\(^11c\) but selective C-4 mono-arylation may be achieved by slow addition of a solution of the arylboronic acid in aqueous sodium carbonate into a solution of 2 equiv of 2,4-dichloropyrimidine in acetonitrile.\(^17\)

An ongoing project in our laboratories required the establishment of a general methodology for the preparation of differentially and unsymmetrically 4,6-disubstituted pyrimidines 8 and 4-substituted pyrimidines 9 and 10 (Figure 2) with an emphasis on arylated pyrimidines. Herein we report studies on the preparation of series of diverse 4,6-disubstituted 8 and 4-substituted pyrimidines 10, the latter group being obtained \textit{via} reductive dehydrochlorination of 6-chloro-4-arylpyrimidine intermediates 9 which avoids the use of expensive 4-chloropyrimidine precursors.\(^10\)
RESULTS AND DISCUSSION

To initiate our study, optimized conditions for mono-arylation using the Suzuki-Miyaura reaction were established on the dichloropyrimidine (11a) and 2-methyl-1-phenylboronic acid (12b) cross-coupling pair (see Table S1 in SI). Standard well-recognized coupling conditions (Pd(PPh3)4/Na2CO3/iPrOH) were used and thence applied for the preparation of a series of mono-chloro aryl-substituted pyrimidines: 4-phenyl (9a), isomeric tolyl (9b, 9c), isomeric anisyl (9d, 9e, 9f), isomeric fluorophenyl (9g, 9h), and two more highly oxygenated derivatives (9i, 9j) (Table 1). Coupling reactions gave mono-arylated products with the exception of 9b, 9c, 9d, 9f, 9g, and 9h which afforded minor but significant amounts of diarylpyrimidines 8b, 8c, 8d, 8f, 8g, and 8h, respectively. Difficulty in separation of mono- (9c, 9g, and 9h) and di-arylated (8c, 8g, and 8h) materials required converting the mixtures to the hydrodechlorination products (17) which allowed facile separation of 8 from the resulting compound 17 (Table 3) (see SI). All reactions were carried out on 2 g scale. Of some note is the fact that cross-coupling proceeds in the case of 9b despite the presence of an ortho substituent.

Table 1. Suzuki-Miyaura reaction of 4,6-dichloropyrimidine 11

<table>
<thead>
<tr>
<th>11a, R1 = Me</th>
<th>12a, R2 = H</th>
<th>12b, R2 = 2-Me</th>
<th>12c, R2 = 3-Me</th>
<th>12d, R2 = 4-OMe</th>
<th>12g, R2 = 3-F</th>
<th>12e, R2 = 3-OMe</th>
<th>12f, R2 = 4-F</th>
<th>12h, R2 = 3,4-(OCH2O)3</th>
<th>12i, R2 = 3,4,5-(OMe)3</th>
</tr>
</thead>
<tbody>
<tr>
<td>9a, 72%</td>
<td>9b, 69% / 8b, 26%</td>
<td>9c: 8c = 79.21%</td>
<td>9d, 80% / 8d, 11%</td>
<td>9g:8g = 91.9%</td>
<td>9g, 74% / 8g, 23%</td>
<td>9h:8h = 73.27%</td>
<td>9i, 77%</td>
<td>9j, 75%</td>
<td></td>
</tr>
</tbody>
</table>

*All reactions were performed on 2 g scale unless otherwise indicated. *Yield of isolated product. *Reaction was performed on 200 mg scale. *Ratio of 9 and 8 by GC-MS analysis. *Mixture of 9 and 8 was isolated (see SI).
The availability of the 4-substituted 6-chloropyrimidines (9) provided the opportunity for the development of a general synthesis of unsymmetrical 4,6-substituted products 8 (Table 2) and a route for 4-monoarylpyrimidines 17 (Table 3). In the first task, a series of selected systems was explored (Table 2). Thus, using standard cross-coupling conditions, 4-amino (15a), 4-methoxy (15b) and a series of 4-aryl (15c-f) pyrimidines were prepared in high yields. Likewise, a number of available heteroarylboronic acids were subjected to the cross-coupling conditions to furnish an array of interesting 4-amino (16a-g) and 4-aryl-6-heteroarylpyrimidines (16h-j) (Table 2). In the 4-aryl-6-heteroaryl series, both $\pi$-excessive and $\pi$-deficient heterocyclic boronic acids underwent cross-coupling to afford products in good to excellent yields. In the second aim, a selected series of 4-aryl-6-chloropyrimidines were subjected to standard hydrogenation conditions to furnish monoarylated pyrimidines 17a-h and 17j generally in very good yields (Table 3). For reasons not understood, compound 9i failed to undergo the dehydrochlorination reaction.

**Table 2. Suzuki-Miyaura reaction of 4-chloro-6-substituted pyrimidines 13**

<table>
<thead>
<tr>
<th>R1</th>
<th>R2</th>
<th>Yield of isolated product.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ar/HetAr-B(OH)2</td>
<td>Pd[P(C6H5)3]4 (5 mol%)</td>
<td>Na2CO3 (2.5 equiv), iPrOH, H2O reflux, 18-24 h</td>
</tr>
<tr>
<td>15a</td>
<td>Me</td>
<td>&gt;95%b</td>
</tr>
<tr>
<td>15b</td>
<td>MeO</td>
<td>85%b</td>
</tr>
<tr>
<td>15c</td>
<td>Ph</td>
<td>&gt;95%c</td>
</tr>
<tr>
<td>15d</td>
<td>MeO</td>
<td>93%c</td>
</tr>
<tr>
<td>15e</td>
<td>94%c</td>
<td></td>
</tr>
<tr>
<td>15f</td>
<td>MeO</td>
<td>95%c</td>
</tr>
<tr>
<td>16a</td>
<td>BnHN</td>
<td>95%c, 71%d</td>
</tr>
<tr>
<td>16b</td>
<td>BnHN</td>
<td>88%c, 77%d</td>
</tr>
<tr>
<td>16c</td>
<td>BnHN</td>
<td>40%c, 82%d</td>
</tr>
<tr>
<td>16d</td>
<td>BnHN</td>
<td>43%c, 51%d</td>
</tr>
<tr>
<td>16e</td>
<td>BnHN</td>
<td>77%c, 45%d</td>
</tr>
<tr>
<td>16f</td>
<td>BnHN</td>
<td>90%c, 48%d</td>
</tr>
<tr>
<td>16g</td>
<td>BnHN</td>
<td>90%c, 61%d</td>
</tr>
<tr>
<td>16h</td>
<td>MeO</td>
<td>&gt;95%c</td>
</tr>
<tr>
<td>16i</td>
<td>MeO</td>
<td>&gt;95%c</td>
</tr>
<tr>
<td>16j</td>
<td>MeO</td>
<td>86%c</td>
</tr>
</tbody>
</table>

aYield of isolated product. b1.1 equiv of organoborane (14), reflux conditions in sealed microwave vial. c1.3 equiv of organoborane (14), reflux conditions in sealed microwave vial. d1.0 equiv of organoborane (14), reflux conditions in a flask.
In summary, this work has shown the value of the venerable Suzuki-Miyaura cross-coupling strategy for the provision of diverse mono-arylated 6-chloropyrimidine derivatives (Table 1) and thereby a conduit to the preparation of unsymmetrical 4,6-diarylated pyrimidines (Table 2). Hydrodechlorination of the 6-chloro derivatives provides an effective alternative route to 4-arylpyrimidines which avoids the use of the very expensive 4-chloropyrimidine starting material. Scale up to gram quantities of most reactions has been demonstrated. The obtained products may be of value in consideration of biological activity (structural analogues of 3, 4, and 5 are kinase inhibitors) and electroluminescent properties. The use of the synthesized pyrimidines in a related project in our laboratories will be reported in due course.

**EXPERIMENTAL**

**General information:** Melting points were obtained on an Electrothermal IA9100 Melting Point Apparatus and are uncorrected. \(^1\)H and \(^13\)C spectra were recorded on Bruker Avance-400 MHz spectrometer. The chemical shifts of \(^1\)H and \(^13\)C NMR signals are quoted relative to internal CHCl\(_3\) (δ = 7.26) and CDCl\(_3\) (δ = 77.0) or tetramethylsilane (δ = 0.0). Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m) and broad singlet (brs). The GC-MS analyses were performed on an Agilent 6890 GC coupled with an Agilent 5973 inert MS under EI conditions. High resolution mass spectra were obtained on a GCT Mass Spectrometer (Waters, Micromass) and a QSTAR XL hybrid mass Spectrometer (Applied Biosystems/MDS Sciex). IR spectra were recorded on a Bruker Alpha FT-IR spectrometer. Column chromatography was performed using silica gel (230-400 mesh) as the stationary phase. All reactions

### Table 3. Hydrodechlorination reaction of 6-chloropyrimidines derivatives 9

<table>
<thead>
<tr>
<th>R(^1)</th>
<th>R(^2)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl</td>
<td></td>
<td>9</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>17a</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17b</td>
<td>67%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17c</td>
<td>&gt;95%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17d</td>
<td>89%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17e</td>
<td>&gt;95%</td>
</tr>
<tr>
<td></td>
<td>OMe</td>
<td>17f</td>
<td>&gt;95%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17g</td>
<td>93%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17h</td>
<td>&gt;95%</td>
</tr>
<tr>
<td></td>
<td>OMe</td>
<td>17i</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Yield of isolated product. \(^b\)Mixture of 9c:8c = 79:21 (GC-MS analysis) was used as SM. \(^c\)Mixture of 9g:8g = 91:9 (GC-MS analysis) was used as SM. \(^d\)Mixture of 9h:8h = 73:27 (GC-MS analysis) was used as SM. \(^e\)SM was recovered in >90% yield.
were monitored by thin layer chromatography (TLC). All reagents and solvents were purchased from commercial sources and used without purification. N-Benzyl-6-chloropyrimidin-4-amine was prepared by a reported procedure.20

**General Procedure for the Synthesis of 6-Aryl-4-chloropyrimidines (9a-j):** To a degassed solution of 4,6-dichloropyrimidine (200 mg, 1.0 equiv) and arylboronic acid (1.0 equiv) in iPrOH (4 mL) in a 20 mL microwave vial was added an aqueous solution of 2M Na₂CO₃ (2.5 equiv) and Pd(PPh₃)₄ (5.0 mol%) under an argon atmosphere and the resulting heterogeneous solution was further degassed for 10 min. The vial was sealed and placed in an oil bath at 83 °C and the reaction mixture was refluxed for 18 h, cooled, diluted with H₂O (20 mL) and the whole was extracted with EtOAc (3 X 30 mL). The combined organic extract was washed with brine, dried (Na₂SO₄), and evaporated under reduced pressure give an oil which was purified by gradient column chromatography on silica gel using EtOAc/hexanes as eluent to afford compounds 9a-j.

4-Chloro-2-methyl-6-phenylpyrimidine (9a): Following the General Procedure and purification method using 4,6-dichloro-2-methylpyrimidine (2.0 g, 1.0 equiv), phenylboronic acid (1.5 g, 1.0 equiv), 2M Na₂CO₃ (15.4 mL, 2.5 equiv), and Pd(PPh₃)₄ (709 mg, 5 mol%) in iPrOH (40 mL) provided compound 9a (1.82 g, 72% yield) as a pale yellow solid, mp 71–73 °C (EtOAc/hexanes); FT-IR (neat) νmax 2923, 2853, 1559, 1533, 1450, 747 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.06-8.03 (m, 2H), 7.54-7.47 (m, 4H), 2.77 (s, 3H); 13C NMR (50 MHz, CDCl₃): δ 169.2, 165.8, 161.6, 135.8, 131.4, 129.1, 127.4, 114.0, 26.1 ppm; HRMS (EI) calcd for C₁₁H₉ClN₂ [M] 204.0454, found 204.0446. The physical and spectral data were consistent with those previously reported.21

4-Chloro-2-methyl-6-(2-methylphenyl)pyrimidine (9b): 200 mg scale reaction: Following the General Procedure and purification method using 4,6-dichloro-2-methylpyrimidine (200 mg, 1.0 equiv), 2-methylphenylboronic acid (167 mg, 1.0 equiv) provided compound 9b (185 mg, 69% yield) and compound 8b (45 mg, 26% yield).

2 g scale reaction: Following the General Procedure and purification method using 4,6-dichloro-2-methylpyrimidine (2.0 g, 1.0 equiv), 2-methylphenylboronic acid (167 mg, 1.0 equiv), 2M Na₂CO₃ (15.4 mL, 2.5 equiv), and Pd(PPh₃)₄ (709 mg, 5 mol%) in iPrOH (40 mL) provided compound 9b (1.66 g, 62% yield) and compound 8b (529 mg, 31% yield).

Compound 9b: Colorless oil; FT-IR (neat) νmax 3096, 2962, 1604, 1394, 1153, 908, 753 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.41-7.38 (m, 1H), 7.37-7.33 (m, 1H), 7.29-7.26 (m, 2H), 2.77 (s, 3H), 2.41 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 168.9, 168.7, 160.9, 136.8, 136.1, 131.3, 129.9, 129.4, 126.2, 118.0, 25.9, 20.3 ppm; HRMS (EI) calcd for C₁₁H₁₀ClN₂ [M] 218.0611, found 218.0619.

Compound 8b: Colorless solid; mp 83–85 °C (EtOAc/hexanes); FT-IR (neat) νmax 3079, 2957, 2836,
1601-1394, 1238, 1045, 766 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.49-7.47 (m, 2H), 7.38-7.29 (m, 7H), 2.86 (s, 3H), 2.46 (s, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 167.7, 167.2, 138.4, 135.9, 131.1, 129.5, 129.4, 126.2, 117.9, 26.5, 20.4 ppm; HRMS (EI) calcd for C\(_{19}\)H\(_{18}\)N\(_2\) [M] 274.1470, found 274.1481.

\textbf{4-Chloro-2-methyl-6-(3-methylphenyl)pyrimidine (9c) and 2-methyl-4,6-bis(3-methylphenyl)pyrimidine (8c):} The General Procedure and purification method were followed using 4,6-dichloro-2-methylpyrimidine (2.0 g, 1.0 equiv), 3-methylphenylboronic acid (1.7 g, 1.0 equiv), 2M Na\(_2\)CO\(_3\) (15.4 mL, 2.5 equiv), and Pd(PPh\(_3\))\(_4\) (709 mg, 5 mol\%) in \(i\)PrOH (40 mL) to provide a mixture of 9c and 8c (2.36 g, 9c:8c = 79:21, by GC-MS) as a colorless oil. This mixture was used without further purification in next hydrodechlorination step.

\textit{200 mg scale reaction:} Following the General Procedure and purification method using 4,6-dichloro-2-methylpyrimidine (200 mg, 1.0 equiv), 3-methylphenylboronic acid (167 mg, 1.0 equiv) provided compound 9c (181 mg, 68% yield) along with 74 mg of a mixture (9c:8c = 26:74 by GC-MS analysis).

\begin{align*}
\text{Compound 9c:} & \text{ Colorless oil; FT-IR (neat) } \nu_{\text{max}} \text{ 3060, 2863, 1556, 1535, 1393, 1147 cm}^{-1}; \ \text{\(^1\)H NMR (400 MHz, CDCl\(_3\)): } \delta \text{ 7.86 (s, 1H), 7.80 (d, } J = 7.6 \text{ Hz, 1H), 7.51 (s, 1H), 7.37 (t, } J = 7.6 \text{ Hz, 1H), 7.29 (d, } J = 7.6 \text{ Hz, 1H), 2.77 (s, 3H), 2.43 (s, 3H); } \text{\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): } \delta \text{ 169.1, 166.0, 161.5, 138.8, 135.7, 132.2, 128.9, 127.9, 124.5, 114.0, 26.1, 21.5 ppm; HRMS (EI) calcd for C}_{12}\text{H}_{11}\text{ClN}_2 [M] 218.0611, \text{found 218.0620.}
\end{align*}

\textbf{4-Chloro-6-(4-methoxyphenyl)-2-methylpyrimidine (9d) and 4,6-bis(4-methoxyphenyl)-2-methylpyrimidine (8d):} The General Procedure and purification method were followed using 4,6-dichloro-2-methylpyrimidine (2.0 g, 1.0 equiv), p-methoxyphenylboronic acid (1.9 g, 1.0 equiv), 2M Na\(_2\)CO\(_3\) (15.4 mL, 2.5 equiv), and Pd(PPh\(_3\))\(_4\) (709 mg, 5 mol\%) in \(i\)PrOH (40 mL) to provide compound 9d (2.3 g, 80% yield) and compound 8d (207 mg, 11% yield).

\begin{align*}
\text{Compound 9d:} & \text{ pale yellow solid, mp 74–75 °C (EtOAc/hexanes); FT-IR (neat) } \nu_{\text{max}} \text{ 3078, 2838, 1607, 1558, 1506, 1252, 1152, 1030, 985, 831 cm}^{-1}; \ \text{\(^1\)H NMR (400 MHz, CDCl\(_3\)): } \delta \text{ 8.03 (d, } J = 8.8 \text{ Hz, 2H), 7.46 (s, 1H), 6.99 (d, } J = 8.8 \text{ Hz, 2H), 3.87 (s, 3H), 2.74 (s, 3H); } \text{\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): } \delta \text{ 168.9, 165.3, 162.4, 161.3, 128.9, 128.1, 114.4, 112.9, 55.5, 26.1 ppm; HRMS (EI) calcd for C}_{12}\text{H}_{11}\text{ClN}_2 [M] 234.0560, \text{found 234.0549.}
\end{align*}

\begin{align*}
\text{Compound 8d:} & \text{ Colorless solid, mp 159–160 °C (EtOAc/hexanes) (lit\textsuperscript{22} mp 159–160 °C); \(^1\)H NMR (400 MHz, CDCl\(_3\)): } \delta \text{ 8.08 (d, } J = 8.6 \text{ Hz, 4H), 7.74 (s, 1H), 7.00 (d, } J = 8.6 \text{ Hz, 4H), 3.86 (s, 6H), 2.81 (s, 3H); } \text{\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): } \delta \text{ 168.2, 163.9, 161.7, 130.0, 128.7, 114.2, 108.3, 55.4, 26.5 ppm. The physical and spectral data were consistent with those reported.\textsuperscript{22}}
\end{align*}

4-Chloro-6-(3-methoxyphenyl)-2-methylpyrimidine (9e): Following the General Procedure and
purification method using 4,6-dichloro-2-methylpyrimidine (2.0 g, 1.0 equiv), 3-methoxyphenylboronic acid (1.87 g, 1.0 equiv), 2M Na₂CO₃ (15.4 mL, 2.5 equiv), and Pd(PPh₃)₄ (709 mg, 5 mol%) in iPrOH (40 mL) provided compound 9e (2.16 g, 75% yield) as a colorless solid, mp 69–71 °C (EtOAc/hexanes); FT-IR (neat) νₘₐₓ 3079-3003, 2957-2836, 1601-1394, 1238, 766 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.62-7.61 (m, 1H), 7.59-7.57 (m, 1H), 7.51 (s, 1H), 7.40 (t, J = 7.9 Hz, 1H), 7.07-7.04 (m, 1H), 3.89 (s, 3H), 2.77 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 169.1, 165.6, 161.5, 160.2, 137.2, 130.1, 119.7, 117.4, 114.1, 112.5, 55.5, 26.0 ppm; HRMS (EI) calcd for C₁₂H₁₁ClN₂O [M] 234.0560, found 234.0551.

4-Chloro-6-(3-methoxyphenyl)pyrimidine (9f) and 4,6-bis(3-methoxyphenyl)pyrimidine (8f): Following the General Procedure and purification method using 4,6-dichloropyrimidine (2.0 g, 1.0 equiv), 3-methoxyphenylboronic acid (2.04 g, 1.0 equiv), 2M Na₂CO₃ (16.8 mL, 2.5 equiv), and Pd(PPh₃)₄ (775 mg, 5 mol%) in iPrOH (40 mL) provided compound 9f (1.66 g, 61% yield) and compound 8f (670 mg, 34% yield).

Compound 9f: Colorless solid, mp 92–94 °C (EtOAc/hexanes); FT-IR (neat) νₘₐₓ 3069, 3003, 2979, 2827, 1606, 1425, 1273, 1174, 788 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): 9.01 (s, 1H), 7.72 (s, 1H), 7.65 (s, 1H), 7.59 (d, J = 7.7 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 7.07 (dd, J₁ = 8.2 Hz, J₂ = 2.4 Hz, 1H), 3.89 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 165.5, 161.9, 160.3, 158.9, 136.7, 130.1, 119.6, 117.8, 117.3, 112.3, 55.5 ppm; HRMS (EI) calcd for C₁₁H₉ClN₂O [M] 220.0403, found 220.0409. The physical and spectral data were consistent with those reported.²

Compound 8f: Pale yellow solid, mp 77–78 °C (EtOAc/hexanes); FT-IR (neat) νₘₐₓ 3136, 3000, 2956, 2833, 1571, 1427, 1265, 1040, 749 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 9.30 (s, 1H), 8.06 (s, 1H), 7.72 (t, J = 2.1 Hz, 2H), 7.69-7.67 (m, 2H), 7.43 (t, J = 8.0 Hz, 2H), 7.08-7.05 (m, 2H), 3.91 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 164.5, 160.2, 159.1, 138.4, 130.0, 119.5, 117.0, 113.1, 112.3, 55.5 ppm; HRMS (EI) calcd for C₁₈H₁₆N₂O₂ [M] 292.1212, found 292.1216.

4-Chloro-6-(4-fluorophenyl)-2-methylpyrimidine (9g) and 4,6-bis(4-fluorophenyl)-2-methylpyrimidine (8g): The General Procedure and purification method were followed using 4,6-dichloro-2-methylpyrimidine (2.0 g, 1.0 equiv), 4-fluorophenylboronic acid (1.7 g, 1.0 equiv), 2M Na₂CO₃ (15.4 mL, 2.5 equiv), and Pd(PPh₃)₄ (709 mg, 5 mol%) in iPrOH (40 mL) to provide a mixture of compound 9g and 8g (2.07 g, 9g:8g = 91:9, by GC-MS) which was forwarded to the hydrodechlorination step.

200 mg scale reaction: Following the General Procedure using 4,6-dichloro-2-methylpyrimidine (200 mg, 1.0 equiv), 4-fluorophenylboronic acid (172 mg, 1.0 equiv) and purification by flash chromatography using Et₂O/hexanes provided compound 9g (202 mg, 74% yield) along with 8g (40 mg, 23%).

Compound 9g: Colorless solid, mp 98–100 °C (EtOAc/hexanes); FT-IR (neat) νₘₐₓ 3115, 3030, 2899, 1600,
1396, 1235, 840 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.09-8.06 (m, 2H), 7.50 (s, 1H), 7.21-7.16 (m, 2H), 2.76 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 169.2, 164.9 (d, \(J = 251\) Hz), 164.6, 161.6, 131.9 (d, \(J = 3\) Hz), 129.5 (d, \(J = 9\) Hz), 116.2 (d, \(J = 22\) Hz), 113.6, 26.0 ppm; HRMS (EI) calcd for C\(_{11}\)H\(_8\)ClFN\(_2\) [M] 222.0360, found 222.0368.

Compound 8g: Pale yellow solid, mp 153.1–154.1 °C (EtOAc/hexanes); FT-IR (neat)  \(\nu_{max}\) 3074, 3045, 1600, 1580, 1507, 1227, 847 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.09-8.06 (m, 2H), 7.50 (s, 1H), 7.21-7.16 (m, 2H), 2.76 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 169.2, 164.9 (d, \(J = 251\) Hz), 164.6, 161.6, 131.9 (d, \(J = 3\) Hz), 129.5 (d, \(J = 9\) Hz), 116.2 (d, \(J = 22\) Hz), 113.6, 26.0 ppm; HRMS (EI) calcd for C\(_{11}\)H\(_8\)ClFN\(_2\) [M] 222.0360, found 222.0368.

4-Chloro-6-(3-fluorophenyl)pyrimidine (9h): Following the General Procedure and purification method using 4,6-dichloro-2-methylpyrimidine (2.0 g, 1.0 equiv), 3-fluorophenylboronic acid (1.72 g, 1.0 equiv), 2M Na\(_2\)CO\(_3\) (15.4 mL, 2.5 equiv), and Pd(PPh\(_3\))\(_4\) (709 mg, 5 mol%) in iPrOH (40 mL) provided compound 9h:8h (2.42 g, 73:27, by GCMS) which was forwarded to the hydrodechlorination step.

200 mg scale reaction: Following the General Procedure using 4,6-dichloro-2-methylpyrimidine (200 mg, 1.0 equiv), 3-fluorophenylboronic acid (172 mg, 1.0 equiv) and purification by flash chromatography using Et\(_2\)O/hexanes provided compound 9h (69 mg, 25% yield) along with 158 mg of a mixture 9h:8h = 58:42 (by GC-MS).

Compound 9h: Colorless solid, mp 109–111 °C (Et\(_2\)O/hexanes); FT-IR (neat)  \(\nu_{max}\) 3077, 3015, 2955, 2853, 1560, 1395, 1210, 775 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.83-7.80 (m, 2H), 7.54 (s, 1H), 7.51-7.45 (m, 1H), 7.25-7.19 (m, 1H), 2.78 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 169.3, 164.4 (d, \(J = 11\) Hz), 161.9, 161.7, 138.0 (d, \(J = 7\) Hz), 130.6 (d, \(J = 8\) Hz), 122.8 (d, \(J = 3\) Hz), 118.3 (d, \(J = 3\) Hz), 114.3 (d, \(J = 23\) Hz), 114.1, 25.9 ppm; HRMS (EI) calcd for C\(_{11}\)H\(_8\)ClFN\(_2\) [M] 222.0360, found 222.0355. The physical and spectral data were consistent with those reported.\(^{23}\)

Compound 8h: Colorless solid, mp 150–152 °C (EtOAc/hexanes); FT-IR (neat)  \(\nu_{max}\) 3135, 3005, 2972, 1613, 1452, 1260, 762 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.89-7.82 (m, 5H), 7.54 (s, 1H), 7.51-7.45 (m, 1H), 7.25-7.19 (m, 1H), 2.78 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 168.9, 163.8, 163.3 (d, \(J = 8\) Hz), 130.5 (d, \(J = 8\) Hz), 122.8 (d, \(J = 3\) Hz), 117.7 (d, \(J = 21\) Hz), 114.3 (d, \(J = 23\) Hz), 109.9, 26.4 ppm; HRMS (EI) calcd for C\(_{17}\)H\(_{12}\)F\(_2\)N\(_2\) [M] 282.0969, found 282.0958.

4-(Benzo[d][1,3]dioxol-5-yl)-6-chloro-2-methylpyrimidine (9i): Following the General Procedure and purification method, using 4,6-dichloro-2-methylpyrimidine (2.0 g, 1.0 equiv), 3,4-(methylenedioxy)phenylboronic acid (2.04 g, 1.0 equiv), 2M Na\(_2\)CO\(_3\) (15.4 mL, 2.5 equiv), and Pd(PPh\(_3\))\(_4\) (709 mg, 5 mol%) in iPrOH (40 mL) provided compound 9i (2.32 g, 77% yield) as a colorless solid, mp 148–149 °C (EtOAc/hexanes); FT-IR (neat)  \(\nu_{max}\) 3118, 3062, 2910, 1570, 1406, 1239, 933 cm\(^{-1}\);
1H NMR (400 MHz, CDCl3): δ 7.62-7.58 (m, 2H), 7.42 (s, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.05 (s, 2H), 2.74 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 168.9, 165.0, 161.4, 150.5, 148.6, 129.9, 122.2, 113.1, 108.6, 107.4, 101.8, 26.0 ppm; HRMS (EI) calcd for C12H9ClN2O2 [M] 248.0353, found 248.0361.

4-Chloro-2-methyl-6-(3,4,5-trimethoxyphenyl)pyrimidine (9j): Following the General Procedure and purification method, using 4,6-dichloro-2-methylpyrimidine (2.0 g, 1.0 equiv), phenylboronic acid (2.6 g, 1.0 equiv), 2M Na2CO3 (15.4 mL, 2.5 equiv), and Pd(PPh3)4 (709 mg, 5 mol%) in iPrOH (40 mL) provided compound 9j (2.69 g, 75% yield) as a colorless solid, mp 113–115 °C (EtOAc/hexanes); FT-IR (neat) νmax 3098, 2998, 2834, 1588, 1392, 1126, 707 cm−1; 1H NMR (400 MHz, CDCl3): δ 7.49 (s, 1H), 7.30 (s, 2H), 3.97 (s, 6H), 3.93 (s, 3H), 2.77 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 169.0, 165.3, 161.5, 153.6, 141.1, 131.0, 113.6, 104.6, 60.9, 56.3, 26.0 ppm; HRMS (EI) calcd for C14H15ClN2O3 [M] 294.0771, found 294.0759.

Suzuki-Miyaura Cross-Coupling of N-Benzyl-6-chloropyrimidin-4-amine (13) with Aromatic Boronic Acids (14):

N-Benzyl-6-(2-methylphenyl)pyrimidin-4-amine (15a): Following the General Procedure and purification method, using N-benzyl-6-chloropyrimidin-4-amine (500 mg, 1.0 equiv), 2-methylphenylboronic acid (364 mg, 1.1 equiv), 2M Na2CO3 (3.0 mL, 2.5 equiv), and Pd(PPh3)4 (141 mg, 5 mol%) in iPrOH (10 mL) to provide compound 15a (626 mg, >95% yield) as a colorless viscous oil; FT-IR (neat) νmax 3407, 3247, 3027, 2966, 2869, 1592, 1411, 1354, 978 cm−1; 1H NMR (400 MHz, CDCl3): δ 8.50 (s, 1H), 7.36-7.18 (m, 9H), 6.32 (s, 2H), 4.52 (s, 2H), 2.28 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 162.5, 158.1, 138.9, 135.7, 130.8, 129.1, 128.8, 127.6, 127.4, 125.8, 45.5, 20.1 ppm; HRMS (EI) calcd for C18H17N3 [M] 275.1422, found 275.1433.

4-Methoxy-2-methyl-6-(2-methylphenyl)pyrimidine (15b): Following the General Procedure and purification method, using 4-chloro-6-methoxy-2-methylpyrimidine S1 (1.0 g, 1.0 equiv), 2-methylphenylboronic acid (743 mg, 1.1 equiv), 2M Na2CO3 (7.9 mL, 2.5 equiv), and Pd(PPh3)4 (365 mg, 5 mol%) in iPrOH (20 mL) provided compound 15b (1.15 g, 85% yield) as pale-yellow oil; FT-IR (neat) νmax 3109, 3019, 2951, 1605, 1402, 1370, 1046, 760 cm−1; 1H NMR (400 MHz, CDCl3): δ 7.38-7.36 (m, 1H), 7.32-7.23 (m, 3H), 6.61 (s, 1H), 4.00 (s, 3H), 2.68 (s, 3H), 2.37 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 169.9, 167.8, 167.7, 138.4, 135.8, 130.9, 129.2, 129.0, 125.9, 101.5, 53.6, 26.1, 20.2 ppm; HRMS (EI) calcd for C13H14N2O [M] 214.1106, found 214.1100.

4-(4-Methoxyphenyl)-2-methyl-6-phenylpyrimidine (15c): Following the General Procedure and purification method, using 4-chloro-6-(4-methoxyphenyl)-2-methylpyrimidine 9d (200 mg, 1.0 equiv), phenylboronic acid (136 mg, 1.3 equiv), 2M Na2CO3 (1.1 mL, 2.5 equiv), and Pd(PPh3)4 (49 mg, 5 mol%) in iPrOH (4 mL) provided compound 15c (225 mg, >95% yield) as a pale yellow solid, mp
103–105 °C (EtOAc/hexanes); FT-IR (neat) ν<sub>max</sub> 3060, 3001, 2960, 2836, 1606, 1393, 1254, 833 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.09 (d, J = 8.8 Hz, 4H), 7.80 (s, 1H), 7.51–7.49 (m, 3H), 7.01 (d, J = 8.8 Hz, 4H), 3.86 (s, 3H), 2.84 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 168.4, 164.7, 164.3, 161.8, 137.7, 130.5, 129.8, 128.9, 128.8, 127.3, 114.3, 109.3, 55.4, 26.5 ppm; HRMS (EI) calcd for C<sub>18</sub>H<sub>16</sub>N<sub>2</sub>O [M] 276.1263, found 276.1270.

4,6-Bis(4-methoxyphenyl)-2-methylpyrimidine (15d): Following the General Procedure and purification method, using 4-chloro-6-(4-methoxyphenyl)-2-methylpyrimidine 9d (200 mg, 1.0 equiv), 4-methoxyphenylboronic acid (169 mg, 1.3 equiv), 2M Na<sub>2</sub>CO<sub>3</sub> (1.1 mL, 2.5 equiv), and Pd(PPh<sub>3</sub>)<sub>4</sub> (49 mg, 5 mol%) in iPrOH (4 mL) provided compound 15d (243 mg, 93% yield) as a colorless solid, mp 159–160 °C (EtOAc/hexanes) (lit<sup>22</sup> mp 159–160 °C); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.08 (d, J = 8.6 Hz, 4H), 7.74 (s, 1H), 7.00 (d, J = 8.6 Hz, 4H), 3.86 (s, 6H), 2.81 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 168.2, 163.9, 161.7, 130.0, 128.7, 114.2, 108.3, 55.4, 26.5 ppm. The physical and spectral data were consistent with those reported.<sup>22</sup>

4-(4-Methoxyphenyl)-2-methyl-6-(2-methylphenyl)pyrimidine (15e): The General Procedure and purification method was followed using 4-chloro-6-(4-methoxyphenyl)-2-methylpyrimidine 9d (400 mg, 1.0 equiv), 2-methylphenylboronic acid (302 mg, 1.3 equiv), 2M Na<sub>2</sub>CO<sub>3</sub> (2.1 mL, 2.5 equiv), and Pd(PPh<sub>3</sub>)<sub>4</sub> (99 mg, 5 mol%) in iPrOH (8 mL) to provide compound 15e (466 mg, 94% yield) as pale yellow solid, mp 67–68 °C (EtOAc/hexanes); FT-IR (neat) ν<sub>max</sub> 3065, 2958, 2837, 1605, 1457, 1368, 1254, 1175, 1032, 836, 759 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.08 (d, J = 8.8 Hz, 2H), 7.53 (s, 1H), 7.46–7.44 (m, 1H), 7.37–7.28 (m, 3H), 7.03–6.99 (m, 2H), 3.86 (s, 3H), 2.83 (s, 3H), 2.43 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 167.9, 167.7, 163.7, 161.9, 138.8, 135.9, 131.0, 129.7, 129.3, 129.2, 128.8, 126.1, 114.3, 113.0, 55.4, 26.5, 20.3 ppm; HRMS (ESI) calcd for C<sub>19</sub>H<sub>18</sub>N<sub>2</sub>O [M + H] 290.1419, found 290.1411.

4-(4-Fluorophenyl)-6-(4-methoxyphenyl)-2-methylpyrimidine (15f): Following the General Procedure and purification method, using 4-chloro-6-(4-methoxyphenyl)-2-methylpyrimidine 9d (200 mg, 1.0 equiv), 4-fluorophenylboronic acid (156 mg, 1.3 equiv), 2M Na<sub>2</sub>CO<sub>3</sub> (1.1 mL, 2.5 equiv), and Pd(PPh<sub>3</sub>)<sub>4</sub> (49 mg, 5 mol%) in iPrOH (4 mL) provided compound 15f (249 mg, >95% yield) as a colorless solid, mp 131–132 °C (EtOAc/hexanes); FT-IR (neat) ν<sub>max</sub> 3062, 3049, 2971, 2839, 1599, 1414, 1227, 829 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.12–8.08 (m, 4H), 7.74 (s, 1H), 7.20–7.16 (m, 2H), 7.02–6.99 (m, 2H), 3.87 (s, 3H), 2.82 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 168.4, 164.4 (d, J = 249 Hz), 164.3, 163.4, 161.9, 133.8, 129.7, 129.2 (d, J = 8 Hz), 128.7, 115.9 (d, J = 22 Hz), 114.3, 108.7, 55.4, 26.5 ppm; HRMS (EI) calcd for C<sub>18</sub>H<sub>15</sub>FN<sub>2</sub>O [M] 294.1158, found 294.1158.
Suzuki-Miyaura Cross-Coupling of N-Benzyl-6-chloropyrimidin-4-amine (13) with Heteroaromatic Boronic Acids (14):

**General Procedure: Method A:** In a microwave vial equipped with a stirbar was added a 0.05 M solution of the aryl chloride 13 (1 equiv) in iPrOH and boronic acid 14 (1.3 equiv) with stirring. The resulting solution was degassed with argon for 5 min before adding a 2M aqueous solution of Na₂CO₃ (2.5 equiv). The mixture was degassed for an additional 5 min before adding Pd(PPh₃)₄ (5 mol%), followed by an additional degassing cycle for 10 min before the vial was sealed and heated at 84 °C with stirring for 18 h. Upon consumption of the starting materials (TLC), the reaction mixture was cooled to rt and a solid impurity was removed by suction filtration. The mother liquor was then diluted with water and the whole was extracted with EtOAc. The combined organic extracts were washed with brine, dried (MgSO₄), evaporated to dryness in vacuo and the residue was subjected to flash silica gel column chromatography (conditions vide infra) to give the pure product.

**Method B:** In a round bottom flask equipped with a stirbar was added with stirring a 0.05 M solution of the aryl chloride 13 (1 equiv) in iPrOH and boronic acid 14 (1.0 equiv). The resulting solution was degassed with argon for 5 min before adding a 2M aqueous solution of Na₂CO₃ (2.5 equiv). The mixture was degassed for an additional 5 min before adding Pd(PPh₃)₄ (5 mol%), followed by an additional degassing cycle for 10 min and heating at 84 °C under argon for 18 h. Upon consumption of the starting materials (TLC), the reaction mixture was cooled to rt and a solid impurity was removed by suction filtration. The mother liquor was then diluted with H₂O and the whole was extracted with EtOAc. The combined organic extracts were washed with brine, dried (MgSO₄) and evaporated to dryness in vacuo and the residue was subjected to flash silica gel column chromatography to give product 16.

**N-Benzyl-6-(pyridin-3-yl)pyrimidin-4-amine (16a):** Following the General Procedure (Method A), using N-benzyl-6-chloropyrimidin-4-amine (100 mg, 0.455 mmol, 1.0 equiv) and pyridin-3-ylboronic acid (73 mg, 0.592 mmol), and purification by flash column chromatography (5% MeOH/EtOAc) afforded compound 16a (113 mg, 95% yield).

Following the General Procedure (Method B), using N-benzyl-6-chloropyrimidin-4-amine (200 mg, 1.0 equiv) and pyridin-3-ylboronic acid (119 mg, 1.0 equiv), and purification by flash column chromatography (30% EtOAc/hexanes) afforded compound 16a (170 mg, 71% yield).

**Compound 16a:** Colourless solid, mp 146-147 °C (EtOAc/hexanes); FT-IR (neat) νmax 3248, 3107, 3029, 2917, 2868, 1600, 1415, 700 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 9.17 (s, 1H), 8.66 (d, 1H, J = 3.6 Hz), 8.56 (s, 1H), 8.33 (d, 1H, 7.3 Hz), 8.14 (d, 1H, 7.3 Hz), 7.51 (t, 1H, J = 3.6 Hz), 7.23 (t, 1H, 7.0 Hz), 7.10 (s, 1H), 4.61 (d, 2H, J = 5.1 Hz) ppm; ¹³C NMR (100 MHz, DMSO-d₆): δ 162.9, 158.6, 150.7, 147.6, 139.4, 133.9, 132.7, 128.3, 127.3, 126.8, 123.8, 101.5, 43.5 ppm; HRMS (EI) calcd for C₁₆H₁₄N₄ [M] 262.1218, found 262.1211.
**N-Benzyl-6-(thiophen-3-yl)pyrimidin-4-amine (16b):** Following the General Procedure (Method A), using N-benzyl-6-chloropyrimidin-4-amine (100 mg, 0.455 mmol, 1.0 equiv) and 3-thienylboronic acid (76 mg, 0.592 mmol, 1.3 equiv) and purification by flash column chromatography (40% EtOAc/hexanes) afforded compound 16b (107 mg, 88% yield).

Following the General Procedure (Method B), using N-benzyl-6-chloropyrimidin-4-amine (200 mg, 1.0 equiv) and 3-thienylboronic acid (125 mg, 1.0 equiv) and purification by flash column chromatography (EtOAc/hexanes) afforded compound 16b (188 mg, 77% yield).

**Compound 16b:** Beige solid, mp 148–150 °C (EtOAc/hexanes); FT-IR (neat) $\nu_{\text{max}}$ 3241, 3105, 3028, 2924, 1594, 1513, 1454, 1351, 1230, 1096, 979, 851, 696 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.58 (s, 1H), 7.98 (dd, $J$ = 3.0 Hz, 1.2 Hz, 1H), 7.53 (dd, $J$ = 5.01 Hz, 1.2 Hz, 1H), 7.39-7.28 (m, 6H), 6.58 (s, 1H), 5.47 (brs, 1H), 4.60 (d, $J$ = 5.6 Hz, 2H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 163.1, 158.9, 140.6, 129.0, 127.8, 127.6, 126.6, 125.84, 125.81, 98.8, 76.4, 45.7 ppm; HRMS (El) calcld for C$_{15}$H$_{13}$N$_3$S [M] 267.0830, found 267.0835.

**N-Benzyl-4,5'-bipyrimidin-6-amine (16c):** Following the General Procedure (Method A), using N-benzyl-6-chloropyrimidin-4-amine (100 mg, 0.455 mmol, 1.0 equiv) and pyrimidin-5-ylboronic acid (73 mg, 0.592 mmol, 1.3 equiv), and purification by flash column chromatography (5% MeOH/EtOAc) afforded compound 16c (48 mg, 40% yield).

Following the General Procedure (Method B), using N-benzyl-6-chloropyrimidin-4-amine (200 mg, 0.455 mmol, 1.0 equiv) and pyrimidin-5-ylboronic acid (121 mg, 1.0 equiv), and purification by flash column chromatography (EtOAc/hexanes) afforded compound 16c (196 mg, 82% yield).

**Compound 16c:** Beige solid, mp 178–180 °C (EtOAc/hexanes); FT-IR (neat) $\nu_{\text{max}}$ 3266, 3151, 3030, 2919, 2850, 1599, 1398, 722 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 9.32-9.28 (m, 2H), 8.57 (s, 1H), 8.18 (s, 1H), 7.64-7.54 (m, 1H), 7.34-7.13 (m, 4H), 5.75 (s, 1H), 4.61 (br s, 2H), 3.38 (s, 1H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 159.1, 158.8, 154.9, 131.5, 131.4, 130.6, 128.8, 128.3, 127.3, 126.8, 102.0, 43.4 ppm; HRMS (El) calcld for C$_{15}$H$_{13}$N$_5$ [M] 263.1171, found 263.1174.

**N-Benzyl-6-(furan-2-yl)pyrimidin-4-amine (16d):** Following the General Procedure (Method A), using N-benzyl-6-chloropyrimidin-4-amine (100 mg, 0.455 mmol, 1.0 equiv) and 2-furanylboronic acid (66 mg, 0.592 mmol) and purification by flash column chromatography (20-40% EtOAc/hexanes) afforded compound 16d (49 mg, 43% yield).

Following the General Procedure (Method B), using N-benzyl-6-chloropyrimidin-4-amine (100 mg, 1.0 equiv) and 2-furanylboronic acid (66 mg, 1.0 equiv) and purification by flash column chromatography (EtOAc/hexanes) afforded compound 16d (58 mg, 51% yield).

**Compound 16d:** Colourless solid, mp 159–160 °C (EtOAc/hexanes); FT-IR (neat) $\nu_{\text{max}}$ 3215, 3138, 3028,
2996, 2870, 1612-1422, 1350, 774 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 8.41 (s, 1H), 8.03 (t, 1H, J = 5.8 Hz), 7.86 (s, 1H), 7.33 (d, 4H, J = 4.4 Hz), 7.24 (dq, 1H, J = 8.5 Hz, 4.2 Hz), 7.10 (ad, 1H), 6.83 (brs, 1H), 6.65-6.64 (m, 1H), 4.58 (brs, 2H) ppm; ¹³C NMR (100 MHz, DMSO-d₆): δ 162.6, 158.5, 151.9, 144.9, 139.4, 128.3, 127.2, 126.8, 112.2, 110.6, 98.2, 43.4 ppm; HRMS (EI) calcd for C₁₅H₁₃N₃O [M] 251.1059, found 251.1066.

N-Benzyl-6-(quinolin-3-yl)pyrimidin-4-amine (16e): Following the General Procedure (Method A), using N-benzyl-6-chloropyrimidin-4-amine (100 mg, 0.455 mmol, 1.0 equiv) and 3-quinolinylboronic acid (102 mg, 0.592 mmol) and purification by flash column chromatography (60% EtOAc/hexanes) afforded compound 16e (109 mg, 77% yield).

Following the General Procedure (Method B), using N-benzyl-6-chloropyrimidin-4-amine (100 mg, 1.0 equiv) and 3-quinolinylboronic acid (79 mg, 1.0) and purification by flash column chromatography (EtOAc/hexanes) afforded compound 16e (64 mg, 45% yield).

Compound 16e: Colourless solid, mp 99–100 °C (EtOAc/hexanes); FT-IR (neat) νmax 3246, 3204, 3029, 2979, 2917, 1595, 1453, 750 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 9.48 (s, 1H), 8.96 (s, 1H), 8.60 (s, 1H), 8.13-8.06 (m, 3H), 7.83-7.79 (m, 1H), 7.66 (t, 1H, J = 7.4 Hz), 7.37-7.32 (m, 4H), 7.24 (t, 2H, J = 7.0 Hz), 4.64 (d, 2 H, J = 5.7 Hz) ppm; ¹³C NMR (100 MHz, DMSO-d₆): δ 158.7, 148.5, 148.1, 139.3, 133.4, 131.5, 131.4, 130.5, 129.9, 129.0, 128.8, 128.7, 128.3, 127.3, 127.20, 127.16, 126.8, 43.5 ppm; HRMS (EI) calcd for C₂₀H₁₆N₄ [M] 312.1375, found 312.1368.

N-Benzyl-6-(1H-indol-5-yl)pyrimidin-4-amine (16f): Following the General Procedure (Method A), using N-benzyl-6-chloropyrimidin-4-amine (100 mg, 0.455 mmol, 1.0 equiv) and 1H-indol-5-ylboronic acid (96 mg, 0.592 mmol, 1.3 equiv) and purification by flash column chromatography (60–70% EtOAc/hexanes) afforded compound 16f (123 mg, 90% yield).

Following the General Procedure (Method B), using N-benzyl-6-chloropyrimidin-4-amine (100 mg, 1.0 equiv) and 1H-indol-5-ylboronic acid (74 mg, 1.0 equiv) and purification by flash column chromatography (EtOAc/hexanes) afforded compound 16f (65 mg, 48% yield).

Compound 16f: Colorless solid, mp 222–224 °C (EtOAc/hexanes); FT-IR (neat) νmax 3236, 3204, 3059, 1594, 1420, 741 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 11.29 (s, 1H), 8.51 (s, 1H), 8.29 (s, 1H), 7.83-7.78 (m, 2H), 7.49 (d, 1H, J = 8.5 Hz), 7.41-7.32 (m, 4H), 7.24 (t, 1H, J = 6.9 Hz), 7.02 (s, 1H), 6.55 (s, 1H), 4.62 (d, 2H, J = 5.4 Hz); ¹³C NMR (100 MHz, DMSO-d₆): δ 163.0, 161.7, 158.2, 139.7, 137.1, 128.3, 128.2, 127.8, 127.2, 126.8, 126.4, 119.7, 118.8, 111.5, 102.1, 99.6, 43.6 ppm; HRMS (EI) calcd for C₁₉H₁₆N₄ [M] 312.1375, found 300.1382.

N-Benzyl-6-(1-methyl-1H-pyrazol-4-yl)pyrimidin-4-amine (16g): Following the General Procedure (Method A), using N-benzyl-6-chloropyrimidin-4-amine (100 mg, 0.455 mmol, 1.0 equiv) and
1-methyl-1\textit{H}-pyrazole-4-boronic acid pinacol ester (123 mg, 0.592 mmol, 1.3 equiv) and purification by flash column chromatography (10% MeOH/EtOAc) afforded compound \textbf{16g} (109 mg, 90% yield). Following the General Procedure (Method B), using \textit{N}-benzyl-6-chloropyrimidin-4-amine (100 mg, 1.0 equiv) and 1-methyl-1\textit{H}-pyrazole-4-boronic acid pinacol ester (95 mg, 1.0 equiv) and purification by flash column chromatography (MeOH/EtOAc) afforded compound \textbf{16g} (74 mg, 61% yield).

**Compound \textbf{16g}:** colourless solid, mp 155–156 °C (EtOAc/hexanes); FT-IR (neat) \(\nu_{\text{max}}\) 3244, 3106, 3028, 2927, 2855, 1597-1413, 1205, 982 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 8.46\) (s, 1H), \(7.91-7.87\) (m, 2H), \(7.42-7.27\) (m, 5H), \(6.42\) (s, 1H), \(5.76\) (br s, 1H), \(4.57\) (s, 2H), \(3.91\) (s, 3H) ppm; \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 162.8, 158.5, 157.4, 137.9, 137.0, 129.9, 128.9, 127.8, 127.5, 122.1, 76.5, 45.6, 39.3\) ppm; HRMS (EI) calcd for C\(_{15}\)H\(_{15}\)N\(_5\) [M] 265.1327, found 265.1322.

\textbf{4-(4-Methoxyphenyl)-6-(thienyl-3-yl)pyrimidine (16h):} Following the General Procedure (Method A), using 4-chloro-6-(4-methoxyphenyl)-2-methylpyrimidine (600 mg, 1.0 equiv) and 3-thienylboronic acid (426 mg, 1.3 equiv), and the resulting mixture was purified by flash chromatography (5\(\rightarrow\)15% EtOAc/hexanes) to afford the product \textbf{16h} (700 mg, 97 % yield) as a pale-yellow solid, mp 104-106 °C (EtOAc:hexanes); FT-IR (neat) \(\nu_{\text{max}}\) 3108, 2836, 1607, 1580, 1512, 1253, 1174, 834 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 8.14\) (d, \(J = 3\) Hz, 1H), \(8.08\) (d, \(J = 8.8\) Hz, 2H), \(7.73\) (d, \(J = 5.1\) Hz, 1H), \(7.66\) (s, 1H), \(7.43\) (dd, \(J = 5.0\) Hz, 3.0 Hz, 1H), \(7.02\) (d, 8.8 Hz, 2H), \(3.87\) (s, 3H), \(2.80\) (s, 3H) ppm; \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 168.6, 164.4, 161.9, 160.3, 140.9, 130.0, 128.88, 126.8, 126.4, 126.2, 114.4, 108.9, 55.5, 26.6\) ppm; HRMS (EI) calcd for C\(_{16}\)H\(_{14}\)N\(_2\)OS [M] 282.0827, found 282.0820.

\textbf{5-(6-(4-Methoxyphenyl)-2-methylpyrimidin-4-yl)-1\textit{H}-indole (16i):} Following the General Procedure (Method A), using 4-chloro-6-(4-methoxyphenyl)-2-methylpyrimidine (175 mg, 1.0 equiv) and 5-indolylboronic acid (156 mg, 1.3 equiv), and the resulting mixture was purified by flash chromatography (40% EtOAc/hexanes) to afford the product \textbf{16i} (232 mg, 98% yield) as a pale-yellow solid, mp 244–245 °C (EtOAc:hexane); FT-IR (neat) \(\nu_{\text{max}}\) 3200, 3180, 1644, 1619, 1603, 140.9, 130.0, 128.88, 126.8, 126.4, 126.2, 114.4, 108.9, 55.5, 26.6 ppm; HRMS (EI) calcd for C\(_{20}\)H\(_{17}\)N\(_3\)O [M] 315.1372, found 315.1379.

\textbf{4-(4-Methoxyphenyl)-2-methyl-6-(pyridin-3-yl)pyrimidine (16j):} Following the General Procedure (Method A), using 4-chloro-6-(4-methoxyphenyl)-2-methylpyrimidine (175 mg, 0.748 mmol) and 3-pyridineboronic acid (120 mg, 0.972 mmol) and purification by flash column chromatography (60% EtOAc/hexanes) afforded compound \textbf{16j} (179 mg, 86% yield) as a beige solid, mp 165–166 °C.
(EtOAc:hexane); FT-IR (neat) $\nu_{\text{max}}$ 3155, 3005, 2839, 1610, 1412, 1248, 1029 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.28 (d, 1H, $J = 1.7$ Hz), 8.72 (dd, 1H, $J = 4.8$ Hz, 1.5 Hz), 8.42 (dt, 1H, $J = 8.0$ Hz, 1.9 Hz), 8.11 (d, 2H, $J = 8.9$ Hz), 7.82 (s, 1H), 7.44 (dd, 1H, $J = 7.9$ Hz, 4.8 Hz), 7.02 (d, 2H, 8.9 Hz), 3.87 (s, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.9, 164.7, 162.2, 162.1, 151.4, 148.7, 134.8, 133.4, 129.5, 128.9, 123.8, 114.5, 109.2, 55.6, 26.6 ppm; HRMS (EI) calcd for C$_{17}$H$_{15}$N$_3$O [M] 277.1215, found 277.1221.

**General Procedure for Hydrodechlorination Reaction of 6-Chloropyrimidines (9a-j):** A round bottom flask was evacuated, backfilled with argon and then charged sequentially with Pd/C (80 mg, 5 wt% on activated carbon), EtOH (4 mL), Et$_3$N (1.1 equiv) and chloropyrimidine 9a-j (200 mg, 1.0 equiv). The reaction vessel was evacuated and backfilled with hydrogen thrice and the reaction mixture was stirred for 4 h under hydrogen atmosphere at rt before passing through a pad of Celite followed by a wash with CH$_2$Cl$_2$. The filtrate was evaporated and the crude reaction mixture was purified by column chromatography on silica gel using EtOAc/hexanes as eluent to afford compounds 17a-j.

**2-Methyl-4-phenylpyrimidine (17a):** Following the General Procedure and purification method, using the chloropyrimidine 9a (1.8 g, 1.0 equiv), Pd/C (760 mg, 5 wt% on activated carbon) and Et$_3$N (1.42 mL, 1.1 equiv) in EtOH (25 mL) afforded compound 17a (1.33 g, 88% yield) as a colorless solid, mp 54–55 °C (EtOAc/hexanes) (lit. mp 55–56 °C); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.65 (d, $J = 5.3$ Hz, 1H), 8.08-8.06 (m, 2H), 7.50-7.48 (m, 4H), 2.80 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.4, 164.1, 157.5, 136.9, 130.8, 128.9, 127.2, 113.9, 26.3 ppm. The physical and spectral data were consistent with those reported.

**2-Methyl-4-(2-methylphenyl)pyrimidine (17b):** Following the General Procedure and purification method, using the chloropyrimidine 9b (200 mg, 1.1 equiv) afforded compound 17b (146 mg, 87% yield) as a colorless oil; FT-IR (neat) $\nu_{\text{max}}$ 3099, 3022, 2961, 2858, 1604, 1392, 754 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.66 (d, $J = 5.2$ Hz, 1H), 7.43-7.40 (m, 1H), 7.35-7.26 (m, 3H), 7.20 (d, $J = 5.2$ Hz, 1H), 2.79 (s, 3H), 2.40 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 167.9, 167.2, 156.8, 137.9, 135.9, 131.1, 129.4, 129.3, 126.1, 117.9, 26.3, 20.3 ppm; HRMS (EI) calcd for C$_{12}$H$_{12}$N$_2$ [M] 184.1000, found 184.1006.

**2-Methyl-4-(3-methylphenyl)pyrimidine (17c) and 2-methyl-4,6-bis(3-methylphenyl)pyrimidine (8c):** Following the General Procedure and purification method, using the chloropyrimidine mixture (2.293 g, 9c:8c = 79:21, by GCMS), Pd/C (876 mg, 5 wt% on activated carbon) and Et$_3$N (1.63 mL, 1.1 equiv) in EtOH (25 mL) afforded compound 9c (1.43 g, >95% yield) and compound 8c (175 mg). Compound 17c: pale yellow oil; FT-IR (neat) $\nu_{\text{max}}$ 3035, 2922, 1572, 1548, 1435, 1312 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.61 (d, $J = 5.3$ Hz, 1H), 7.89 (s, 1H), 7.81 (d, $J = 7.7$ Hz, 1H), 7.43 (d, $J = 5.3$ Hz, 1H), 7.28 (m, 1H), 2.79 (s, 3H), 2.11 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 167.9, 167.2, 156.8, 137.9, 135.9, 131.1, 129.4, 129.3, 126.1, 117.9, 26.3, 20.3 ppm; HRMS (EI) calcd for C$_{12}$H$_{12}$N$_2$ [M] 184.1000, found 184.1006.
Hz, 1H), 7.36 (t, J = 7.7 Hz, 1H), 7.28 (d, J = 7.7 Hz, 1H), 2.79 (s, 3H), 2.42 (s, 3H); ^13^C NMR (100 MHz, CDCl₃): δ 168.3, 164.5, 157.3, 138.6, 136.9, 131.6, 128.8, 127.8, 124.3, 113.9, 26.3, 21.5 ppm; HRMS (EI) calcd for C₁₂H₁₂N₂ [M] 184.1000, found 184.1009.

Compound 8c: Pale yellow solid, mp 65–67 °C (EtOAc/hexanes); FT-IR (neat) ν_{max} 3038, 2922, 1571, 1534, 1487, 793 cm⁻¹; ^1^H NMR (400 MHz, CDCl₃): δ 7.95 (s, 2H), 7.89 (d, J = 7.7 Hz, 2H), 7.85 (s, 1H), 7.40 (t, J = 7.7 Hz, 2H), 7.31 (d, J = 7.7 Hz, 2H), 2.87 (s, 3H), 2.46 (s, 6H); ^13^C NMR (100 MHz, CDCl₃): δ 168.5, 164.9, 138.7, 137.5, 131.4, 128.8, 127.9, 124.4, 110.2, 26.6, 21.6 ppm; HRMS (EI) calcd for C₁₉H₁₈N₂ [M] 274.1470, found 274.1481.

4-(4-Methoxyphenyl)-2-methylpyrimidine (17d): Following the General Procedure and purification method, using the chloropyrimidine 9d (2.0 g, 1.0 equiv), Pd/C (760 mg, 5 wt% on activated carbon) and Et₃N (1.31 mL, 1.1 equiv) in EtOH (25 mL) afforded compound 17d (1.53 g, 89% yield) as a colorless solid, mp 109–111 °C (EtOAc/hexanes) (lit²⁵ mp 110–112 °C); ^1^H NMR (400 MHz, CDCl₃): δ 8.58 (d, J = 5.4 Hz, 1H), 8.05 (d, J = 8.8 Hz, 2H), 7.41 (d, J = 5.4 Hz, 1H), 6.99 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H), 2.77 (s, 3H); ^13^C NMR (100 MHz, CDCl₃): δ 168.2, 163.5, 161.9, 157.1, 129.3, 128.7, 114.3, 113.0, 55.4, 26.3 ppm. The physical and spectral data were consistent with those previously reported.²⁵

4-(3-Methoxyphenyl)-2-methylpyrimidine (17e): Following the General Procedure and purification method, using the chloropyrimidine 9e (2.16 g, 1.0 equiv), Pd/C (750 mg, 5 wt% on activated carbon) and Et₃N (1.41 mL, 1.1 equiv) in EtOH (25 mL) afforded compound 17e (1.81 g, 98% yield) as a colorless solid, mp 33–35 °C (EtOAc/hexanes); FT-IR (neat) ν_{max} 3075, 3029, 2958, 2835, 1601, 1390, 1180 cm⁻¹; ^1^H NMR (400 MHz, CDCl₃): δ 8.66 (d, J = 5.4 Hz, 1H), 7.67-7.65 (m, 1H), 7.63-7.60 (m, 1H), 7.49 (d, J = 5.4 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 7.06-7.03 (m, 1H), 3.90 (s, 3H), 2.80 (s, 3H); ^13^C NMR (100 MHz, CDCl₃): δ 168.3, 163.7, 160.1, 157.4, 138.3, 129.9, 119.5, 116.7, 114.0, 112.3, 55.4, 26.3 ppm; HRMS (EI) calcd for C₁₂H₁₂N₂O [M] 200.0950, found 200.0941.

4-(3-Methoxyphenyl)pyrimidine (17f): Following the General Procedure and purification method, using the chloropyrimidine 9f (1.5 g, 1.0 equiv), Pd/C (550 mg, 5 wt% on activated carbon) and Et₃N (1.04 mL, 1.1 equiv) in EtOH (25 mL) afforded compound 17f (1.24 g, 98% yield) as a colorless oil; FT-IR (neat) ν_{max} 3077, 3005, 2957, 2835, 1601, 1428, 1386, 1230, 770 cm⁻¹; ^1^H NMR (400 MHz, CDCl₃): δ 9.26 (d, J = 1.4 Hz, 1H), 8.75 (d, J = 5.3 Hz, 1H), 7.71-7.68 (m, 2H), 7.64-7.61 (m, 1H), 7.42 (t, J = 8 Hz, 1H), 7.08-7.04 (m, 1H), 3.90 (s, 3H); ^13^C NMR (100 MHz, CDCl₃): δ 163.7, 160.2, 159.1, 157.5, 137.9, 130.0, 119.5, 117.2, 117.1, 112.1, 55.4 ppm; HRMS (EI) calcd for C₁₁H₁₀N₂O [M] 186.0793, found 186.0799. The physical and spectral data were consistent with those reported.²⁶

4-(4-Fluorophenyl)-2-methylpyrimidine (17g) and 4,6-bis(4-fluorophenyl)-2-methylpyrimidine (8g): Following the General Procedure and purification method, using the chloropyrimidine mixture (2.0 g,
Compound 17g: pale yellow solid, mp 69–70 °C (EtOAc/hexanes); FT-IR (neat) $\nu_{\text{max}}$ 3119, 2933, 1600, 1548, 1441, 1232, 1168, 837 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.64 (d, $J = 5.4$ Hz, 1H), 8.10–8.05 (m, 2H), 7.43 (d, $J = 5.4$ Hz, 1H), 7.19–7.14 (m, 2H), 2.78 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.4, 164.5 (d, $J = 249$ Hz), 162.8, 157.5, 133.0 (d, $J = 3$ Hz), 129.1 (d, $J = 9$ Hz), 115.9 (d, $J = 21$ Hz), 113.5, 26.3 ppm; HRMS (EI) calcd for C$_{11}$H$_9$FN$_2$ [M] 188.0750, found 188.0741.

Compound 8g: pale yellow solid, mp 153.1–154.1 °C (EtOAc/hexanes); FT-IR (neat) $\nu_{\text{max}}$ 3074, 3045, 1600, 1580, 1441, 1232, 1168, 837 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): 8.15–8.10 (m, 4H), 7.78 (s, 1H), 7.23–7.17 (m, 4H), 2.83 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.6, 164.5 (d, $J = 249.5$ Hz), 163.8, 133.5 (d, $J = 3.3$ Hz), 129.3 (d, $J = 8.7$ Hz), 116.0 (d, $J = 21.6$ Hz), 109.2, 26.5 ppm; HRMS (EI) calcd for C$_{17}$H$_{12}$F$_2$N$_2$ [M] 282.0969, found 282.0961.

4-(3-Fluorophenyl)-2-methylpyrimidine (17h) and 4,6-bis(3-fluorophenyl)-2-methylpyrimidine (8h):

Following the General Procedure and purification method, using the chloropyrimidine mixture (2.3 g, 9h:8h = 73:27, by GCMS), Pd/C (600 mg, 5 wt% on activated carbon) and Et$_3$N (1.16 mL, 1.1 equiv) in EtOH (25 mL) afforded compound 17h (1.39 g, 97% yield) and compound 8h (490 mg).

Compound 17h: colorless solid, mp 67–69 °C (EtOAc/hexanes); FT-IR (neat) $\nu_{\text{max}}$ 3129, 3019, 2998, 2916, 1613, 1435, 1203, 768 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.68 (d, $J = 5.3$ Hz, 1H), 7.84–7.81 (m, 2H), 7.49–7.44 (m, 2H), 7.22–7.17 (m, 1H), 2.80 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.6, 164.3 (d, $J = 245$ Hz), 162.6, 157.7, 139.3 (d, $J = 8$ Hz), 130.5 (d, $J = 8$ Hz), 122.7 (d, $J = 3$ Hz), 117.7 (d, $J = 21$ Hz), 114.2 (d, $J = 23$ Hz), 113.9, 26.3 ppm; HRMS (EI) calcd for C$_{11}$H$_9$FN$_2$ [M] 188.0750, found 188.0742.

Compound 8h: colorless solid, mp 150–152 °C (EtOAc/hexanes); FT-IR (neat) $\nu_{\text{max}}$ 3135, 3005, 2972, 2856, 1613, 1452, 1260, 762 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.15–8.10 (m, 4H), 7.78 (s, 1H), 7.23–7.17 (m, 4H), 2.83 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.9, 163.8, 163.3 (d, $J = 245$ Hz), 162.1, 139.6 (d, $J = 8$ Hz), 130.5 (d, $J = 8$ Hz), 122.8 (d, $J = 3$ Hz), 117.7 (d, $J = 21$ Hz), 114.2 (d, $J = 23$ Hz), 113.9, 26.3 ppm; HRMS (EI) calcd for C$_{17}$H$_{12}$F$_2$N$_2$ [M] 282.0969, found 282.0958.

2-Methyl-4-(3,4,5-trimethoxyphenyl)pyrimidine (17j):

Following the General Procedure and purification method, using the chloropyrimidine 9j (2.5 g, 1.0 equiv), Pd/C (700 mg, 5 wt% on activated carbon) and Et$_3$N (1.3 mL, 1.1 equiv) in EtOH (25 mL) afforded compound 17j (2.06 g, 93% yield) as a colorless solid, mp 94–96 °C (EtOAc/hexanes); FT-IR (neat) $\nu_{\text{max}}$ 3075, 2996, 2957, 2835, 1590, 1427, 1341, 1125, 767 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.64 (d, $J = 1.3$ Hz, 1H), 7.45 (d, $J = 1.3$ Hz, 1H), 7.33 (s, 2H), 3.97 (s, 6H), 3.92 (s, 3H), 2.80 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.3,
163.5, 157.4, 153.6, 140.6, 132.3, 113.6, 104.4, 60.9, 56.3, 26.3 ppm; HRMS (EI) calcd for \( \text{C}_{14}\text{H}_{16}\text{N}_{2}\text{O}_{3} \) [M] 260.1161, found 260.1170.

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REFERENCES AND NOTES


9. For selective examples of cross-coupling reactions on several heterocyclic systems, see: (a) K.
10. At the time of writing, 4,6-dichloropyrimidine: 50 g/$474 and 4-chloropyrimidine: 25 mg/$163 from Sigma-Aldrich.


