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Transition Metal Free Intermolecular Direct Oxidative C−N Bond Formation to Polysubstituted Pyrimidines Using Molecular Oxygen as the Sole Oxidant

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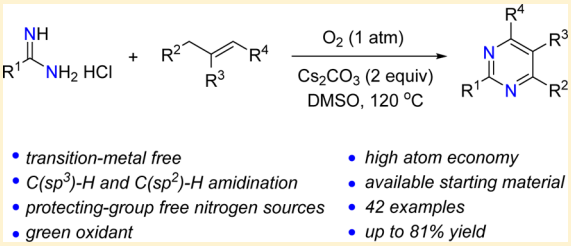
Supporting Information

ABSTRACT: Various polysubstituted pyrimidines are smoothly formed via a base-promoted intermolecular oxidation C−N bond formation of allylic C(sp^3)−H and vinylic C(sp^2)−H of allylic compounds with amidines using O_2 as the sole oxidant. This protocol features protecting group free nitrogen sources, good functional group tolerance, high atom economy, and environmental advantages.



INTRODUCTION

Pyrimidines represent important building blocks in natural products, agrochemicals, pharmaceuticals, and functional materials.[1] They also are used in a wide range of applications as anti-inflammatory, antimicrobial, and antimalarial agents, cytotoxic inhibitors, and photophysical materials.[2] A number of synthetic routes have also been developed for the synthesis of pyrimidines through the cascade condensation cyclization−oxidation of amidines with 1,3-dicarbonyl derivatives, α,β-unsaturated ketones, propargylic alcohols, and propargylamines, and reaction of α,α-dibromo oxime ethers with Grignard reagents.[3] Movassaghi et al. reported a single-step procedure for the synthesis of primidines from *N*-vinyl amides and nitriles using 2-chloropyridine with trifluoromethanesulfonic anhydride as amide activation reagents (Scheme 1, a).[4] Campagne et al. found the transformation of Cbz-protected β-enaminones with amides into 2,4,6-trisubstituted pyrimidines (Scheme 1, b).[5] Recently, Kempe et al. developed an iridium-catalyzed multicomponent synthesis of pyrimidines from amidines and up to three (different) alcohols (Scheme 1, c).[6] Konakahara et al. also successfully synthesized 4,5-disubstituted pyrimidine derivatives via a $ZnCl_2$-catalyzed three-component coupling reaction of enamines, triethyl orthoformate, and ammonium acetate.[7] However, most of the methods mentioned above suffered from one or more drawbacks such as harsh reaction conditions (special reaction medium and reagents, microwave irradiation, and transition metals) and starting materials that require multistep synthesis. Therefore, the development of simple and efficient procedures for acquisition of pyrimidines from easily available starting materials under mild conditions continues to attract the interest of organic chemists because of the remarkable application value of the targeting materials.

Direct C−H amination has emerged as a powerful synthetic protocol for the C−N bond-forming reactions and the construction of *N*-heterocycles, avoiding the preinstallation of transformable functional groups and proceeding with atom economy and environmental sustainability.[8] Many attractive approaches have been dominant in the presence of transition metal catalysts, Pd,[9] Rh,[10] Cu,[11] Ni,[12] and Au,[13] involving intra- or intermolecular amination processes. Meanwhile, most of the preactivated or preoxidized amination substrates bearing strong electron-withdrawing groups, such as *N*-carboxylates,[10,14] *N*-tosylates,[13,15] *N*-nosyloxy-carbamates,[16] *N*-halides,[17] *N*-fluorobenzenesulfonimides,[18] di-*tert*-butyldiaziridinones,[19] azides,[20] and diaziridine,[21] are universal for these transformations. Despite all the progress in transition metal-catalyzed C−H amination, the moisture sensitivity, environmental toxicity, and cost-effectiveness as well as the residual transition metal impurities in the final products remain a major problem, affecting the practical applicability, especially in the preparation of pharmaceutical agents and functional materials.[22] In this particular aspect, the alternative transition metal free direct C−H amination is a worthwhile assignment. In some pioneering examples, the intermolecular aminations were mediated, catalyzed, and/or promoted by hypervalent iodine(III) reagents,[23] bromide,[24] NIS,[25] H_2O_2,[26] DTBP,[27] and TBHP.[28] However, the use of overstoichiometric amounts of oxidants is also expensive and would produce a large amount of byproducts.

For green and sustainable chemistry, molecular oxygen (O_2) is considered to be an ideal oxidant because of its natural, inexpensive, and environmentally friendly characteristics and

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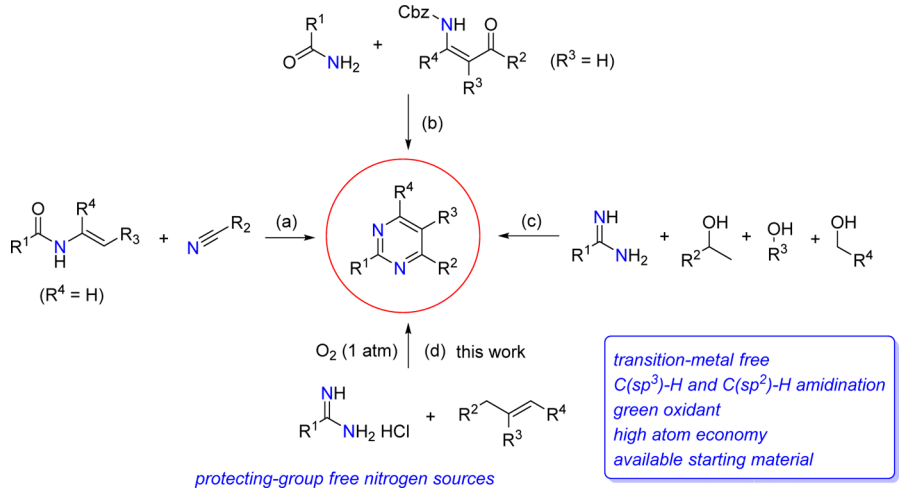
Scheme 1. Synthesis of Polysubstituted Pyrimidines



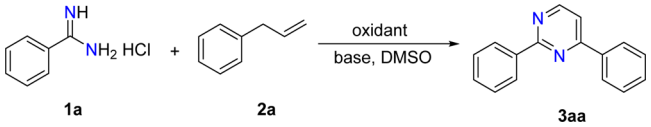
therefore shows attractive academic and industrial prospects.[29] In the past few years, our group has developed a series of C−H activation reactions using O_2 as the terminal oxidant,[30] and we envision that the employment of O_2 could be applied to the allylic C−H amination. Herein, we disclose a base-promoted intermolecular oxidation C−N bond formation of allylic C(sp^3)−H and vinylic C(sp^2)−H of allyllic compounds with amidines to afford polysubstituted pyrimidines using O_2 as the sole oxidant, in which amidines were used as naked nitrogen sources without any protecting groups (Scheme 1, d).

RESULTS AND DISCUSSION

We initially chose easily accessible benzamidine (**1a**) with allylbenzene (**2a**) as the model substrates to test the feasibility of our process (Table 1). Fortunately, the desired product (**3aa**) was obtained in DMSO in the presence of a base and an oxygen atmosphere. Some conclusions could be drawn from the results. (i) Inorganic bases such as K_3PO_4, KOH, and Cs_2CO_3 facilitated the transformation, with the strong bases being the best choice (Table 1, entries 1−4). (ii) Other organic bases that were screened inhibited this reaction process (Table 1, entries 7−12). (iii) A lower temperature led to a decreased yield (Table 1, entries 5 and 6). (iv) Both the base and O_2 were found to be indispensable (Table 1, entries 13 and 14). (v) Other oxidants, such as TBHP, DTBP, H_2O_2, $K_2S_2O_8$, *p*-BQ, and DDQ, have been examined; however, they did not enhance the yield of the target product, and O_2 was found to be an efficient green oxidant (Table 1, entries 15−20). (vi) The yields of **3aa** with other solvents such as DMF, toluene, and dioxane were lower than that with DMSO (Table 1, entries 21−23). Overall, **3aa** was successfully formed in 85% GC yield under the optimized conditions [Cs_2CO_3 (2 equiv) and O_2 (1 atm) in DMSO at 120 °C] (Table 1, entry 4).

The reaction generality and the scope of the metal free reaction process were next explored under the optimized conditions. As summarized in Table 2, various amidines were employed as simple synthetic blocks to react with allylbenzenes to generate an array of 2,4-disubstituted pyrimidines. Generally, arylamidines bearing either electron-donating or electron-withdrawing groups are efficient substrates, providing the desired products (**3aa**−**3la**) in good yields. Gratifyingly, a moderate yield of **3ea** was observed when 4-nitrobenzimidamide was used in this amidination reaction. Isonicotinamidine, nicotinamidine, and picolinamidine could also be transformed in combination with allylbenzene into the desired products (**3ma**−**3oa**) in moderate yields upon isolation. Nonaromatic amidines were also tolerated well, delivering the desired products (**3pa**−**3sa**) in moderate yields. It is noteworthy that an important pharmaceutical intermediate (**3ra**)[2c,31] was successfully obtained from guanidine and allylbenzene. This transformation provides an opportunity for further selective functionalization at the amino group in the

Table 1. Selected Optimization Studies[a]



1a 2a 3aa

entry	base	oxidant[b]	*T* (°C)	yield (%)[c]
1	K_2CO_3	O_2	120	28
2	K_3PO_4	O_2	120	55
3	KOH	O_2	120	80
4	Cs_2CO_3	O_2	120	85
5	Cs_2CO_3	O_2	100	63
6	Cs_2CO_3	O_2	80	34
7	$(CH_3)_3COK$	O_2	120	26
8	CH_3ONa	O_2	120	19
9	DBU	O_2	120	10
10	DABCO	O_2	120	trace
11	Et_3N	O_2	120	12
12	pyridine	O_2	120	nd
13	–	O_2	120	nd
14[d]	Cs_2CO_3	–	120	nd
15[d]	Cs_2CO_3	TBHP	120	16
16[d]	Cs_2CO_3	DTHP	120	nd
17[d]	Cs_2CO_3	35% H_2O_2	120	18
18[d]	Cs_2CO_3	$K_2S_2O_8$	120	trace
19[d]	Cs_2CO_3	*p*-BQ	120	trace
20[d]	Cs_2CO_3	DDQ	120	trace
21[e]	Cs_2CO_3	O_2	120	41
22[f]	Cs_2CO_3	O_2	120	trace
23[g]	Cs_2CO_3	O_2	120	trace

[a]Unless otherwise noted, all reactions were performed with **1a** (0.25 mmol), **2a** (0.30 mmol), an oxidant (0.25 mmol), and a base (2 equiv) in 1.0 mL of DMSO for 24 h. [b]O_2 was used at 1 atm. [c]GC yield based on **1a** with *n*-dodecane as an internal standard. [d]Under vacuum. [e]DMF as the solvent. [f]Toluene as the solvent. [g]1,4-Dioxane as the solvent.

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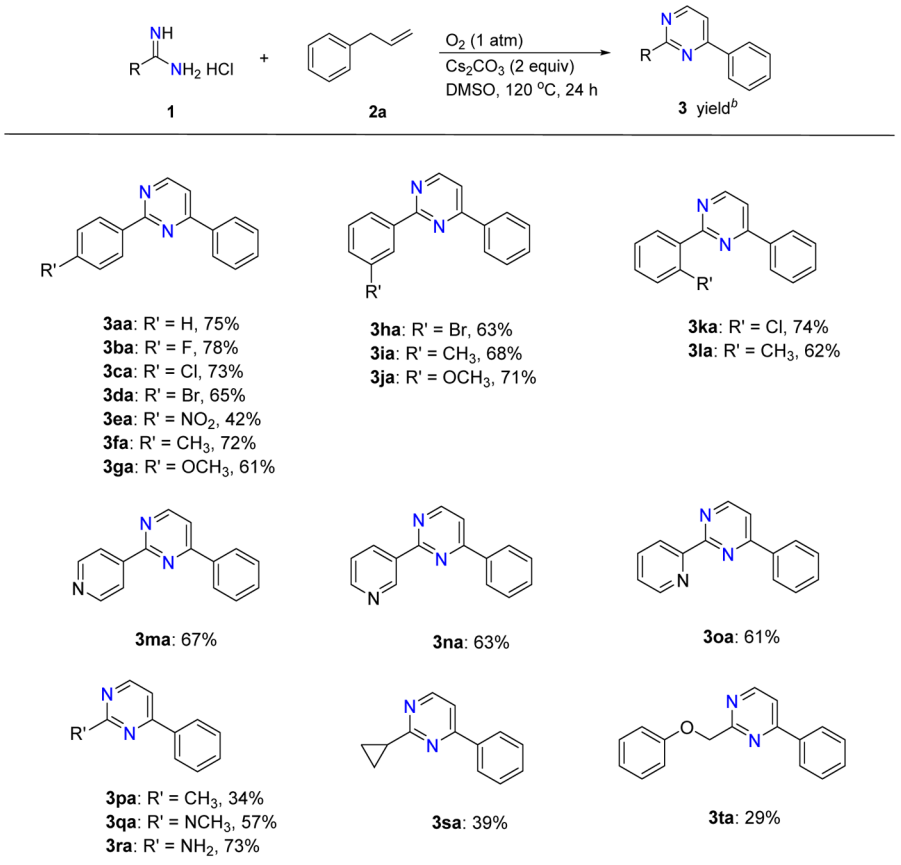
Table 2. Substrate Scope of Amidines[a]



[a]Unless otherwise noted, all reactions were performed with **1** (0.25 mmol), **2a** (0.30 mmol), and a base (2 equiv) in 1.0 mL of DMSO under an O_2 atmosphere for 24 h. [b]Yields of isolated products.

design and screening of pharmaceuticals and agrochemicals. However, for 2-phenoxyacetamidine, an only 29% yield of the desired product (**3ta**) was obtained.

The scope of the allylic substrates is also crucial for the extensive utility of this amidination method. Under the same optimized conditions, the generality of the aryl allylic substrates is summarized in Table 3. The reactions involving *para*-, *meta*-, and *ortho*-substituted allylbenzenes were found to give the desired products in good yields (**3ab**−**3ak**), but the substrate with the electron-donating substituent was less reactive than that with the electron-withdrawing substituent in this transformation. Moreover, disubstituted and trisubstituted allylbenzenes were applicable to this transformation, affording the desired products in moderate yields (**3al**−**3an**). Interestingly, to the allylbenzene derivatives with more than one allylic group, the reaction occurred on only one aryl allylic group because of the conjugative effect and the other remained (**3ao** and **3ap**). Heteroaryl-substituted propenes such as 2-allylfuran (**2q**) and 2-allylthiophene (**2r**) also produced the desired products in fair yields. To our delight, 1-naphthylpropene could be converted to the corresponding product in 53% yield (**3as**). Interestingly, the transformation of (2-methylallyl)benzene proceeded efficiently under the optimized conditions and afforded the desired product (**3at**) in a moderate yield. In particular, the substitution with benzyl groups at α- and γ-positions of the terminal alkene delivered the products (**3au**) in 81% yield, which might be attributed to the formation of macro π-conjugation systems, promoting the amidination process.[32] Moreover, the substitution by CH_3 at the γ-position of the (*E*)-but-2-en-1-ylbenzene (**2v**) generated the desired products (**3av**) in moderate yield. However, the substitution with a benzyl group at the β-position of prop-2-ene-1,2-diyldibenzene afforded a trace of products because of the steric effect.

Furthermore, nonaryl-allylic compounds **2w** and **2x** were also reacted with **1a** to give the same product 2-phenylpyrimidine (**3aw**). These reactions likely proceed through a different mechanism, involving nucleophilic substitution and then oxidation−amination−cyclization processes (Scheme 2). The alkyl- or cyclic-allylic compounds were examined and found to be unsuitable substrates for the reaction under current conditions.

Several control experiments were conducted to gain more insight into the mechanism of this unique reaction. In the presence of 1,1-diphenylethylene (DPE) under the standard reaction conditions, the yield of **3aa** dropped to 14%. Moreover, when 2,6-di-*tert*-butyl-4-methylphenol (BHT) was added, no **3aa** could be detected. These results suggested that a possible radical pathway should be involved (Scheme 3, a). Furthermore, *N*-cinnamylbenzimidamide (**4**) was used as the substrate under the same conditions, and the desired product (**3aa**) was obtained in 83% yield, indicating that **4** might be a reasonable intermediate (Scheme 3, b).

On the basis of the experimental observations mentioned above and previous reports,[33] we propose a possible mechanism for the reaction shown in Scheme 4. This mechanism involves (i) deprotonation of benzamidine under strong basic conditions to give intermediate **A**, (ii) oxidation of **A** by O_2 via a single-electron

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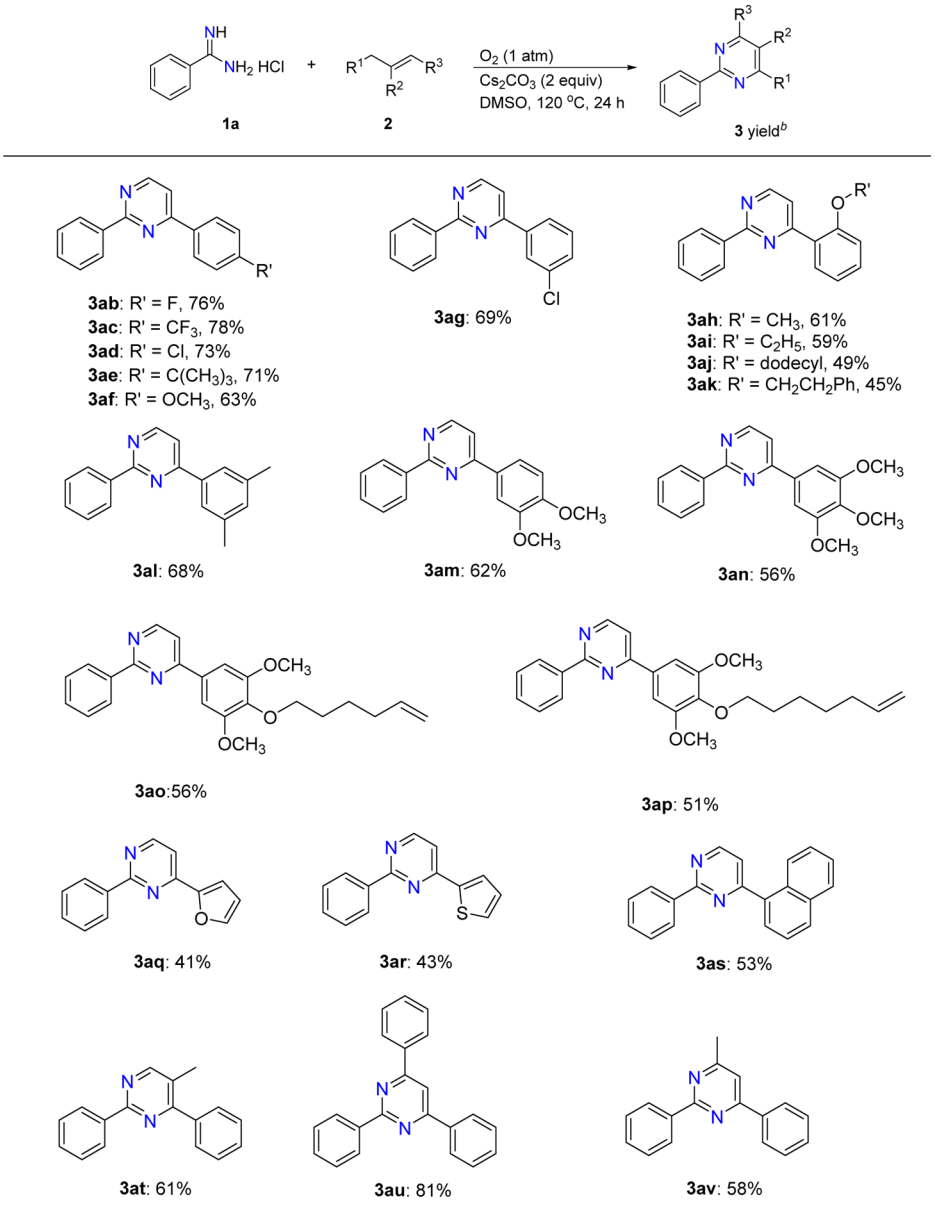
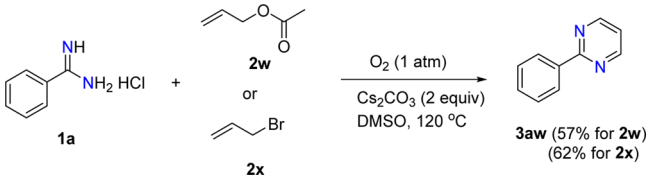
Table 3. Substrate Scope of Aryl Allylic Substrates[a]

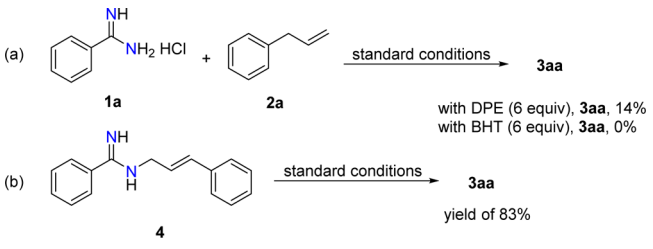


[a]All reactions were performed with **1a** (0.25 mmol), **2** (0.3 mmol), and Cs_2CO_3 (2 equiv) in 1.0 mL of DMSO under an O_2 atmosphere (1 atm) for 24 h. Isolated yield based on **2a**. [b]Yields of isolated products.

Scheme 2. Scope of Non-Aryl-allylic Compounds



Scheme 3. Mechanistic Studies



transfer (SET) process to deliver a superoxide anion radical and benzamidinyl radical intermediate **B**, (iii) oxidation of **2a** through abstraction of a benzylic hydrogen to generate a highly stabilized benzylic/allylic radical, which then undergoes coupling with the intermediate **B** to give **4**, and (iv) intermediate **4** undergoing the deprotonation−oxidation−addition and aromatization process to afford desired product **3aa**.

CONCLUSION

In conclusion, this protocol realizes a base-promoted intermolecular oxidation amidination reaction of allylic compounds with amidines under an oxygen atmosphere. This observation provides a novel route for the oxidation amidination of C(sp^3)−

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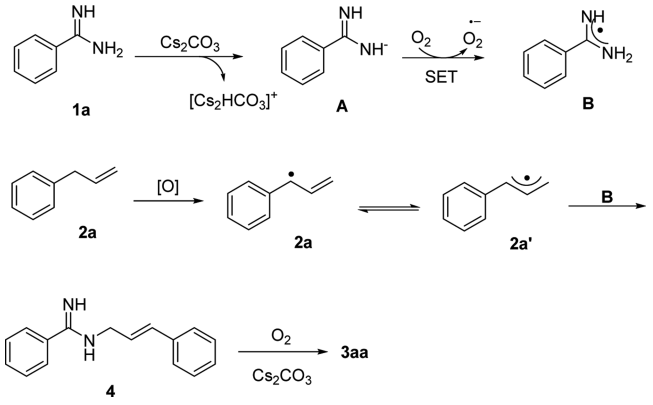
Scheme 4. Proposed Mechanism



H and C(sp^2)−H bonds of allylic compounds simultaneously using protecting group free nitrogen sources. This transformation allows the synthesis of a wide variety of polysubstituted pyrimidines and prevents the use of toxic metals or an overstoichiometric amount of oxidants, which also shows high atom economy, good functional group tolerance, and environmental advantages.

EXPERIMENTAL SECTION

General Information. Melting points were measured using a melting point instrument and are uncorrected. ^{1}H and ^{13}CNMR spectra were recorded on a 400 MHz NMR spectrometer. IR spectra were obtained with an infrared spectrometer on either potassium bromide pellets or liquid films between two potassium bromide pellets. GC−MS data were obtained using electron ionization. HRMS was conducted on a high-resolution mass spectrometer. TLC was performed using commercially available 100−400 mesh silica gel plates (GF_{254}). Unless otherwise noted, purchased chemicals were used without further purification.

General Procedure for Synthesis of Polysubstituted Pyrimidines. A mixture of amidines (0.25 mmol), allylic compounds (0.30 mol), and Cs_2CO_3 (0.50 mmol, 2 equiv) was stirred in DMSO (1.0 mL) under 1 atm of O_2 at 120 °C for 24 h. After completion of the reaction (monitored by TLC), water (10 mL) was added to the reaction mixture, and the resulting mixture was extracted with ethyl acetate. The combined organic layers were then dried over $MgSO_4$, filtered, and then concentrated in vacuum. The residue was purified by flash chromatography on silica gel to give the desired product (using the mixture of petroleum ether and ethyl acetate as eluents).

*2,4-Diphenylpyrimidine (**3aa**).*[34] White solid: 75% yield (43 mg); mp 63−65 °C; IR (KBr) 3064, 1563, 1422, 1383, 1182, 1068, 1030, 747, 691; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78−8.77 (m, 1H), 8.59−8.58 (m, 2H), 8.19−8.18 (m, 2H), 7.52−7.49 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 163.9, 157.9, 137.9, 137.0, 131.0, 130.8, 129.0, 128.6, 128.4, 127.2, 114.5; MS (EI, 70 eV) m/z 232.13, 129.11, 116.16, 102.08; HRMS (ESI) calcd for $C_{16}H_{13}N_2$ $[M + H]^+$ m/z 233.1073, found m/z 233.1070.

*2-(4-Fluorophenyl)-4-phenylpyrimidine (**3ba**).*[35] White solid: 78% yield (49 mg); mp 72−74 °C; IR (KBr) 3064, 1601, 1566, 1433, 1403, 1224, 1187, 1066, 1037, 841, 768, 691; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78−8.77 (m, 1H), 8.59−8.58 (m, 2H), 8.19−8.18 (m, 2H), 7.54−7.51 (m, 4H), 7.19−7.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8 (d, J = 249 Hz), 163.9, 163.7, 157.9, 136.9, 134.1 (d, J = 3 Hz), 131.1, 130.4 (d, J = 9 Hz), 129.0, 127.2, 115.5 (d, J = 21 Hz), 114.4; MS (EI, 70 eV) m/z 250.14, 129.13, 121.09, 102.10; HRMS (ESI) calcd $C_{16}H_{12}FN_2$ $[M + H]^+$ m/z 251.0979, found m/z 251.0977.

*2-(4-Chlorophenyl)-4-phenylpyrimidine (**3ca**).*[36] White solid: 73% yield (48 mg); mp 117−119 °C; IR (KBr) 3050, 1601, 1566, 1437, 1354, 1089, 841, 767, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, J = 8.0 Hz, 1H), 8.51 (d, J = 8.0 Hz, 2H), 8.19−8.18 (m, 2H), 7.54−7.45 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 163.6, 157.9, 136.9, 136.8, 136.4, 131.1, 129.7, 129.0, 128.8, 127.2, 114.7; MS (EI, 70 eV) m/z 266.11, 137.04, 129.10, 115.13, 102.08; HRMS (ESI) calcd $C_{16}H_{12}ClN_2$ $[M + H]^+$ m/z 267.0684, found m/z 267.0685.

*2-(4-Bromophenyl)-4-phenylpyrimidine (**3da**).*[37] White solid: 78% yield (49 mg); mp 151−153 °C; IR (KBr) 3053, 1601, 1547, 1432, 1370, 1070, 836, 767, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78−8.77 (m, 1H), 8.44 (d, J = 8.0 Hz, 2H), 8.19−8.18 (m, 2H), 7.63−7.52 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 163.7, 157.9, 136.8, 136.7, 131.7, 131.1, 129.9, 129.0, 127.2, 125.5, 114.8; MS (EI, 70 eV) m/z 310.07, 231.17, 181.01, 155.06, 129.13, 102.10; HRMS (ESI) calcd $C_{16}H_{12}BrN_2$ $[M + H]^+$ m/z 311.0178, found m/z 311.0182.

*2-(4-Nitrophenyl)-4-phenylpyrimidine (**3ea**).* Yellow solid: 42% yield (29 mg); mp 223−225 °C; IR (KBr) 3064, 1636, 1547, 1412, 1348, 1036, 852, 739; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89−8.88 (m, 1H), 8.77−8.74 (m, 2H), 8.35 (d, J = 8.0 Hz, 2H), 8.22−8.21 (m, 2H), 7.70−7.69 (m, 1H), 7.57−7.56 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 162.5, 158.1, 149.3, 143.6, 136.4, 131.4, 129.2, 129.1, 127.3, 123.7, 115.6; MS (EI, 70 eV) m/z 277.16, 247.17, 231.16, 207.10, 129.11, 102.08; HRMS (ESI) calcd $C_{16}H_{12}N_3O_2$ $[M + H]^+$ m/z 278.0924, found m/z 278.0925.

*4-Phenyl-2-(p-tolyl)pyrimidine (**3fa**).*[36] White solid: 72% yield (44 mg); mp 85−87 °C; IR (KBr) 3064, 2954, 1549, 1432, 1373, 1068, 833, 766, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72−8.71 (m, 1H), 8.47 (d, J = 8.0 Hz, 2H), 8.16−8.15 (m, 2H), 7.46−7.45 (m, 4H), 7.29 (d, J = 8.0 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 163.8, 157.8, 141.0, 137.1, 135.3, 130.9, 129.4, 128.9, 128.3, 127.2, 114.3, 21.6; MS (EI, 70 eV) m/z 246.18, 129.12, 117.12, 102.10; HRMS (ESI) calcd $C_{17}H_{15}N_2$ $[M + H]^+$ m/z 247.1230, found m/z 247.1230.

*2-(4-Methoxyphenyl)-4-phenylpyrimidine (**3ga**).*[35] White solid: 61% yield (40 mg); mp 83−85 °C; IR (KBr) 3015, 2838, 1603, 1510, 1402, 1302, 1250, 1170, 1028, 821, 771, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 8.0 Hz, 1H), 8.53 (d, J = 8.0 Hz, 2H), 8.09−8.08 (m, 2H), 7.40−7.39 (m, 3H), 7.32−7.31 (m, 1H), 6.96 (d, J = 8.0 Hz, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 163.5, 162.0, 157.8, 137.0, 130.9, 130.7, 130.0, 128.9, 127.2, 113.9, 113.8, 55.3; MS (EI, 70 eV) m/z 262.15, 247.13, 219.15, 133.12, 102.11; HRMS (ESI) calcd $C_{17}H_{15}N_2O$ $[M + H]^+$ m/z 263.1179, found m/z 263.1177.

*2-(3-Bromophenyl)-4-phenylpyrimidine (**3ha**).*[37] Yellow liquid: 63% yield (49 mg); IR (KBr) 3058, 1549, 1438, 1367, 1069, 842, 761, 686; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68−8.65 (m, 2H), 8.44 (d, J = 8.0 Hz, 1H), 8.08−8.07 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H), 7.44−7.41 (m, 4H), 7.29 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 163.0, 157.8, 139.9, 136.5, 133.6, 131.3, 131.2, 130.1, 129.0, 127.2, 126.9, 122.9, 114.9; MS (EI, 70 eV) m/z 310.06, 231.06129.12, 115.26, 102.09; HRMS (ESI) calcd $C_{16}H_{12}BrN_2$ $[M + H]^+$ m/z 311.0178, found m/z 311.0178.

*4-Phenyl-2-(m-tolyl)pyrimidine (**3ia**).* Colorless liquid: 68% yield (42 mg); IR (KBr) 3052, 2928, 1641, 1568, 1436, 1367, 1065, 1036, 962, 852, 764, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72−8.71 (m, 1H), 8.39−8.38 (m, 2H), 8.15−8.14 (m, 2H), 7.44−7.36 (m, 5H), 7.28−7.26 (m, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 163.8, 157.8, 138.2, 137.9, 137.0, 131.6, 131.0, 129.0, 128.5, 127.3, 125.6, 114.5, 21.6; MS (EI, 70 eV) m/z 246.03, 129.02, 117.01, 102.01; HRMS (ESI) calcd $C_{17}H_{15}N_2$ $[M + H]^+$ m/z 247.1230, found m/z 247.1234.

*2-(3-Methoxyphenyl)-4-phenylpyrimidine (**3ja**).*[37] Colorless liquid: 71% yield (46 mg); IR (KBr) 3057, 2954, 1641, 1565, 1433, 1376, 1280, 1229, 1073, 1040, 844, 765, 689; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.20−8.14 (m, 4H), 7.47−7.39 (m, 5H), 7.03 (d, J = 8.0 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 163.8, 160.0, 157.8, 139.4, 136.9, 131.0, 129.6, 129.0, 127.2, 120.9, 117.0, 114.6, 113.2, 55.4; MS (EI, 70 eV) m/z 261.15, 232.17, 131.16, 103.11; HRMS (ESI) calcd $C_{17}H_{15}N_2O$ $[M + H]^+$ m/z 263.1179, found m/z 263.1180.

*2-(2-Chlorophenyl)-4-phenylpyrimidine (**3ka**).*[38] White solid: 74% yield (49 mg); mp 70−72 °C; IR (KBr) 3053, 1619, 1540, 1437, 1365, 1072, 848, 754, 692; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, J = 8.0 Hz, 1H), 8.16−8.15 (m, 2H), 7.86 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.50−7.47 (m, 4H), 7.36−7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 164.0, 157.7, 137.9, 136.6, 133.0, 132.0, 131.2, 130.7, 130.5, 129.0, 127.4, 126.8, 114.7; MS (EI, 70 eV) m/z 266.12, 231.15,

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J. Org. Chem. 2016, 81, 5538−5546

137.05, 129.11, 102.09; HRMS (ESI) calcd $C_{16}H_{12}ClN_2$ $[M + H]^+$ m/z 267.0684, found m/z 267.0686.

4-Phenyl-2-(o-tolyl)pyrimidine (**3la**).[37] Colorless oil: 62% yield (38 mg); IR (KBr) 3056, 2959, 1642, 1559, 1426, 1374, 1068, 1039, 926, 844, 752, 692; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80−8.79 (m, 1H), 8.15−8.14 (m, 2H), 7.97−7.96 (m, 1H), 7.53−7.46 (m, 4H), 7.33−7.31 (m, 3H), 2.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 163.5, 157.7, 138.4, 137.5, 136.9, 131.5, 131.0, 130.8, 129.5, 129.0, 127.3, 126.0, 113.9, 21.6; MS (EI, 70 eV) m/z 245.18, 168.15, 121.62, 103.12; HRMS (ESI) calcd $C_{17}H_{15}N_2$ $[M + H]^+$ m/z 247.1230, found m/z 247.1233.

4-Phenyl-2-(pyridin-4-yl)pyrimidine (**3ma**).[37] Yellow solid: 67% yield (39 mg); mp 118−120 °C; IR (KBr) 3062, 1709, 1642, 1607, 1578, 1549, 1421, 1383, 1058, 838, 795, 691; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81−8.77 (m, 3H), 8.38−8.37 (m, 2H), 8.18−8.17 (m, 2H), 7.63−7.62 (m, 1H), 7.52−7.51 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 162.5, 158.0, 150.4, 145.1, 136.3, 131.3, 129.0, 127.2, 122.1, 115.9; MS (EI, 70 eV) m/z 233.14, 205.15, 129.12, 102.11; HRMS (ESI) calcd $C_{15}H_{12}N_3$ $[M + H]^+$ m/z 234.1026, found m/z 234.1029.

4-Phenyl-2-(pyridin-3-yl)pyrimidine (**3na**). Yellow solid: 63% yield (37 mg); mp 78−81 °C; IR (KBr) 3055, 1715, 1645, 1565, 1544, 1428, 1373, 1037, 829, 794, 694; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 8.79−8.71 (m, 3H), 8.17−8.16 (m, 2H), 7.58−7.57 (m, 1H), 7.51−7.50 (m, 3H), 7.42−7.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 162.8, 157.9, 151.3, 150.0, 136.4, 135.5, 133.3, 131.2, 129.0, 127.2, 123.3, 115.1; MS (EI, 70 eV) m/z 233.15, 207.15, 129.13, 102.13; HRMS (ESI) calcd $C_{15}H_{12}N_3$ $[M + H]^+$ m/z 234.1026, found m/z 234.1029.

4-Phenyl-2-(pyridin-2-yl)pyrimidine (**3oa**). Yellow solid: 61% yield (35 mg); mp 65−67 °C; IR (KBr) 3058, 1710, 1643, 1565, 1422, 1382, 1065, 854, 787, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87−8.83 (m, 2H), 8.60 (d, J = 8.0 Hz, 1H), 8.14−8.13 (m, 2H), 7.81−7.77 (m, 1H), 7.57−7.56 (m, 1H), 7.45−7.43 (m, 3H), 7.33−7.32 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 163.4, 158.3, 154.8, 149.8, 136.7, 136.3, 131.0, 128.8, 127.1, 124.7, 123.5, 115.6; MS (EI, 70 eV) m/z 233.16, 205.13, 129.12, 102.13; HRMS (ESI) calcd $C_{15}H_{11}N_3Na$ $[M + Na]^+$ m/z 256.0845, found m/z 256.0850.

2-Methyl-4-phenylpyrimidine (**3pa**).[36] White solid: 34% yield (15 mg); mp 55−56 °C; IR (KBr) 3052, 2954, 1641, 1577, 1548, 1436, 1360, 1315, 1206, 1042, 843, 749, 692; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68−8.65 (m, 1H), 8.06−8.05 (m, 2H), 7.49−7.48 (m, 4H), 2.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 164.1, 157.4, 136.9, 130.8, 128.9, 127.2, 114.0, 26.3; MS (EI, 70 eV) m/z 170.15, 129.12, 102.10; HRMS (ESI) calcd $C_{11}H_{11}N_2$ $[M + H]^+$ m/z 171.0917, found m/z 171.0920.

N-Methyl-4-phenylpyrimidin-2-amine (**3qa**). White solid: 57% yield (26 mg); mp 98−101 °C; IR (KBr) 3416, 3052, 2953, 1642, 1558, 1455, 1342, 816; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34−8.33 (m, 1H), 8.03−8.02 (m, 2H), 7.46−7.45 (m, 3H), 6.96−6.95 (m, 1H), 5.44 (s, 1H), 3.06−3.04 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 163.2, 158.4, 137.5, 130.5, 128.7, 127.0, 106.3, 28.4; MS (EI, 70 eV) m/z 185.15, 156.13, 129.10; HRMS (ESI) calcd $C_{11}H_{12}N_3$ $[M + H]^+$ m/z 186.1026, found m/z 186.1029.

4-Phenylpyrimidin-2-amine (**3ra**).[39] White solid: 73% yield (31 mg); mp 160−161 °C; IR (KBr) 3420, 3056, 1641, 1557, 1434, 1370, 1061, 854; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26−8.25 (m, 1H), 7.92−7.91 (m, 2H), 7.40−7.39 (m, 3H), 6.96−6.95 (m, 1H), 5.30 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 163.3, 158.6, 137.2, 130.6, 128.8, 127.1, 107.7; MS (EI, 70 eV) m/z 170.03, 155.01, 128.03, 102.99; HRMS (ESI) calcd $C_{10}H_{10}N_3$ $[M + H]^+$ m/z 172.0869, found m/z 172.0873.

2-Cyclopropyl-4-phenylpyrimidine (**3sa**).[37] Pale yellow oil: 39% yield (19 mg); IR (KBr) 3063, 2955, 2885, 1645, 1575, 1495, 1442, 1414, 1376, 1186, 1062, 960, 841, 767, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57−8.56 (m, 1H), 8.06−8.05 (m, 2H), 7.46−7.40 (m, 4H), 2.33−2.32 (m, 1H), 1.23−1.22 (m, 2H), 1.09−1.07 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 163.5, 157.2, 137.0, 130.7, 128.8, 127.1, 113.4, 18.4, 10.8; MS (EI, 70 eV) m/z 195.14, 170.14, 129.13, 103.12; HRMS (ESI) calcd $C_{13}H_{13}N_2$ $[M + H]^+$ m/z 197.1073, found m/z 197.1075.

2-(Phenoxymethyl)-4-phenylpyrimidine (**3ta**). Pale yellow oil: 29% yield (19 mg); IR (KBr) 3078, 2923, 2851, 1640, 1577, 1493, 1408, 1311, 1070, 921, 842, 782, 621; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80−8.79 (m, 1H), 8.09−8.08 (m, 2H), 7.62−7.61 (m, 1H), 7.51−7.50 (m, 3H), 7.30−7.26 (m, 2H), 7.07−7.05 (m, 2H), 6.96−6.94 (m, 1H), 5.38 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 164.4, 158.6, 158.1, 136.4, 131.2, 129.4, 129.0, 127.3, 121.1, 115.5, 115.0, 70.9; MS (EI, 70 eV) m/z 262.19, 245.15, 233.18, 185.14, 156.13, 130.14, 115.12, 103.12; HRMS (ESI) calcd $C_{17}H_{15}N_2O$ $[M + H]^+$ m/z 263.1179, found m/z 263.1176.

4-(4-Fluorophenyl)-2-phenylpyrimidine (**3ab**).[35] Yellow solid: 76% yield (47 mg); mp 55−56 °C; IR (KBr) 3065, 1641, 1563, 1426, 1378, 1069, 1034, 829, 758, 694; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53−8.52 (m, 1H), 8.41−8.40 (m, 2H), 7.96−7.95 (m, 2H), 7.33−7.32 (m, 3H), 7.20 (s, 1H), 6.99−6.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7 (d, J = 250 Hz), 164.5, 162.6, 157.8, 137.8, 133.0 (d, J = 3 Hz), 130.8, 129.2 (d, J = 8 Hz), 128.6, 128.4, 115.9 (d, J = 22 Hz), 114.0; MS (EI, 70 eV) m/z 250.16, 147.12, 120.09, 103.11; HRMS (ESI) calcd $C_{16}H_{12}FN_2$ $[M + H]^+$ m/z 251.0979, found m/z 251.0979.

2-Phenyl-4-[4-(trifluoromethyl)phenyl]pyrimidine (**3ac**).[37] Yellow solid: 78% yield (58 mg); mp 75−77 °C; IR (KBr) 3054, 1641, 1557, 1432, 1371, 1327, 1121, 1069, 830, 761, 695; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76−8.75 (m, 1H), 8.54−8.53 (m, 2H), 8.20 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.48−7.44 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (d, J = 250 Hz), 158.2, 140.2, 137.5, 132.5 (dd, J = 33 Hz, J = 97 Hz), 131.0, 128.6, 128.4, 127.5, 125.8 (dd, J = 3 Hz, J = 11 Hz), 125.4, 122.7, 114.7; MS (EI, 70 eV) m/z 300.15, 197.11, 170.11, 150.14, 120.11, 103.10; HRMS (ESI) calcd $C_{17}H_{12}F_3N_2$ $[M + H]^+$ m/z 301.0947, found m/z 301.0954.

4-(4-Chlorophenyl)-2-phenylpyrimidine (**3ad**).[36] Yellow solid: 73% yield (49 mg); mp 70−71 °C; IR (KBr) 3089, 1719, 1642, 1565, 1420, 1384, 1089, 1065, 826, 759, 646; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83−8.82 (m, 1H), 8.56−8.55 (m, 2H), 8.17−8.14 (m, 2H), 7.54−7.48 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 162.7, 158.0, 137.6, 137.3, 135.4, 130.9, 129.2, 128.6, 128.5, 128.3, 114.2; MS (EI, 70 eV) m/z 265.99, 231.03, 163.00, 135.95, 103.01; HRMS (ESI) calcd $C_{16}H_{12}ClN_2$ $[M + H]^+$ m/z 267.0684, found m/z 267.0687.

4-[4-(tert-Butyl)phenyl]-2-phenylpyrimidine (**3ae**). Colorless oil: 71% yield (51 mg); IR (KBr) 3062, 2960, 1612, 1567, 1427, 1379, 1068, 1033, 854, 787, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77−8.76 (m, 1H), 8.59−8.58 (m, 2H), 8.14 (d, J = 8.0 Hz, 2H), 7.52−7.49 (m, 6H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 163.9, 157.7, 154.5, 138.0, 134.2, 130.7, 128.6, 128.3, 127.0, 125.9, 114.3, 34.9, 31.3; MS (EI, 70 eV) m/z 288.23, 273.20, 245.18, 122.62; HRMS (ESI) calcd $C_{20}H_{21}N_2$ $[M + H]^+$ m/z 289.1699, found m/z 289.1698.

4-(4-Methoxyphenyl)-2-phenylpyrimidine (**3af**).[37] White solid: 63% yield (41 mg); mp 87−89 °C; IR (KBr) 3070, 2957, 2844, 1611, 1568, 1511, 1418, 1384, 1285, 1251, 1030, 828, 760, 695; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74−8.73 (m, 1H), 8.57 (d, J = 8.0 Hz, 2H), 8.18 (d, J = 8.0 Hz, 2H), 7.51−7.49 (m, 4H), 7.01 (d, J = 8.0 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 163.4, 162.1, 157.5, 138.0, 130.6, 129.4, 128.8, 128.5, 128.3, 114.3, 113.7, 55.4; MS (EI, 70 eV) m/z 262.16, 247.14, 219.14, 159.13, 132.12, 117.09, 103.09; HRMS (ESI) calcd $C_{17}H_{15}N_2O$ $[M + H]^+$ m/z 263.1179, found m/z 263.1178.

4-(3-Chlorophenyl)-2-phenylpyrimidine (**3ag**).[37] Yellow oil: 69% yield (46 mg); IR (KBr) 3069, 1640, 1559, 1479, 1421, 1380, 1072, 1033, 929, 844, 792, 755, 692; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73−8.72 (m, 1H), 8.54−8.52 (m, 2H), 8.14 (s, 1H), 7.95−7.93 (m, 1H), 7.48−7.32 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 162.3, 158.1, 138.7, 137.6, 135.1, 130.9, 130.9, 130.1, 128.6, 128.4, 127.3, 125.2, 114.5; MS (EI, 70 eV) m/z 265.97, 231.03, 162.99, 135.96, 103.02; HRMS (ESI) calcd $C_{16}H_{12}ClN_2$ $[M + H]^+$ m/z 267.0684, found m/z 267.0683.

4-(2-Methoxyphenyl)-2-phenylpyrimidine (**3ah**).[37] Pale yellow oil: 61% yield (40 mg); IR (KBr) 3061, 2953, 1561, 1490, 1425, 1377, 1257, 1182, 1062, 1027, 843, 751, 696, 620; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74−8.73 (m, 1H), 8.56 (d, J = 8.0 Hz, 2H), 8.23 (d, J = 8.0 Hz, 1H), 7.84−7.83 (m, 1H), 7.48−7.38 (m, 4H), 7.12−7.09 (m, 1H), 6.96−6.94 (m, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 162.6, 158.3, 156.8, 138.2, 131.8, 131.3, 130.5, 128.5, 128.2, 126.4, 121.2, 119.7, 111.6, 56.0; MS (EI, 70 eV) m/z 262.16, 233.17, 157.12, 130.12, 103.06;

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HRMS (ESI) calcd $C_{17}H_{15}N_2O$ $[M + H]^+$ m/z 263.1179, found m/z 263.1180.

*4-(2-Ethoxyphenyl)-2-phenylpyrimidine (**3ai**).* White solid: 59% yield (41 mg); mp 77−79 °C; IR (KBr) 3046, 2929, 1640, 1560, 1539, 1448, 1371, 1260, 1041, 858, 749, 694, 621; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75−8.74 (m, 1H), 8.56 (d, J = 8.0 Hz, 2H), 8.26 (d, J = 8.0 Hz, 1H), 7.91−7.90 (m, 1H), 7.49−7.36 (m, 4H), 7.12−7.10 (m, 1H), 6.95−6.93 (m, 1H), 4.07 (q, J = 4.0 Hz, 2H), 1.40 (t, J = 4.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 162.7, 157.7, 156.8, 138.3, 131.8, 131.3, 130.5, 128.5, 128.2, 126.3, 121.0, 119.6, 112.5, 64.2, 14.9; MS (EI, 70 eV) m/z 276.02, 260.99, 232.04, 220.02, 157.04, 129.03, 103.01, 89.00; HRMS (ESI) calcd $C_{18}H_{16}N_2NaO$ $[M + Na]^+$ m/z 299.1155, found m/z 299.1158.

*4-[2-(Dodecyloxy)phenyl]-2-phenylpyrimidine (**3aj**).* Yellow oil: 49% yield (51 mg); IR (KBr) 3110, 3077, 2926, 2855, 1640, 1563, 1490, 1421, 1382, 1255, 1037, 849, 749, 694, 621; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77−8.76 (m, 1H), 8.57−8.55 (m, 2H), 8.26−8.24 (m, 1H), 7.92−7.91 (m, 1H), 7.49−7.41 (m, 4H), 7.14−7.11 (m, 1H), 7.02−7.00 (m, 1H), 4.07 (t, J = 4.0 Hz, 2H), 1.84−1.81 (m, 2H), 1.45−1.43 (m, 2H), 1.27−1.25 (m, 16H), 0.88 (t, J = 4.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 162.8, 157.8, 156.5, 138.1, 131.7, 131.3, 130.5, 128.5, 128.2, 126.4, 121.0, 119.6, 112.5, 68.7, 31.9, 29.7, 29.6, 29.6, 29.6, 29.4, 29.3, 29.2, 26.2, 22.7, 14.1; MS (EI, 70 eV) m/z 416.12, 280.98, 261.01, 247.99, 206.97, 126.98; HRMS (ESI) calcd $C_{28}H_{36}N_2NaO$ $[M + Na]^+$ m/z 439.2720, found m/z 439.2724.

*4-(2-Phenethoxyphenyl)-2-phenylpyrimidine (**3ak**).* Yellow oil: 45% yield (39 mg); IR (KBr) 3064, 3031, 2952, 2880, 1639, 1565, 1544, 1422, 1382, 1257, 1062, 1029, 853, 749, 698, 622; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59−8.54 (m, 3H), 8.18 (d, J = 8.0 Hz, 1H), 8.49−8.46 (m, 4H), 7.38−7.34 (m, 1H), 7.28−7.20 (m, 5H), 7.10−7.7 (m, 1H), 6.95−6.93 (m, 1H), 4.24 (t, J = 4.0 Hz, 2H), 3.05 (t, J = 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 162.5, 157.4, 156.7, 138.4, 138.2, 131.7, 131.4, 130.5, 129.1, 128.6, 128.6, 128.3, 126.7, 126.7, 121.3, 119.9, 112.5, 69.2, 35.8; MS (EI, 70 eV) m/z 351.06, 261.01, 248.01, 232.04, 219.99, 129.04, 105.03, 77.00; HRMS (ESI) calcd $C_{24}H_{20}N_2NaO$ $[M + Na]^+$ m/z 375.1468, found m/z 375.1472.

*4-(3,5-Dimethylphenyl)-2-phenylpyrimidine (**3al**).*[37] Yellow oil: 68% yield (44 mg); IR (KBr) 3050, 2955, 1617, 1560, 1428, 1367, 1071, 837, 759, 694; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78−8.77 (m, 1H), 8.58−8.57 (m, 2H), 7.81−7.80 (m, 2H), 7.52−7.51 (m, 4H), 7.15−7.14 (m, 1H), 2.44 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 164.3, 157.6, 138.5, 138.0, 137.0, 132.7, 130.7, 128.5, 128.3, 125.1, 114.7, 21.5; MS (EI, 70 eV) m/z 260.21, 157.17, 130.15, 103.11; HRMS (ESI) calcd $C_{18}H_{17}N_2$ $[M + H]^+$ m/z 261.1386, found m/z 261.1384.

*4-(3,4-Dimethoxyphenyl)-2-phenylpyrimidine (**3am**).*[40] White solid: 62% yield (45 mg); mp 115−116 °C; IR (KBr) 3140, 3079, 2956, 2842, 1642, 1563, 1459, 1421, 1389, 1224, 1062, 1024, 840, 759, 697; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73−8.72 (m, 1H), 8.56−8.55 (m, 2H), 7.86 (s, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.50−7.47 (m, 4H), 6.93 (d, J = 8.0 Hz, 1H), 4.01 (s, 3H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 163.3, 157.5, 151.7, 149.4, 138.0, 130.7, 129.6, 128.5, 128.2, 120.4, 113.8, 111.0, 109.9, 56.0, 56.0; MS (EI, 70 eV) m/z 292.21, 277.18, 246.20, 205.13, 146.14, 103.09; HRMS (ESI) calcd $C_{18}H_{17}N_2O_2$ $[M + H]^+$ m/z 293.1285, found m/z 293.1284.

*2-Phenyl-4-(3,4,5-trimethoxyphenyl)pyrimidine (**3an**).* White solid: 56% yield (46 mg); mp 161−163 °C; IR (KBr) 3054, 2953, 1640, 1615, 1563, 1432, 1343, 1127, 829, 757, 700; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77−8.76 (m, 1H), 8.55 (d, J = 8.0 Hz, 2H), 7.49−7.44 (m, 6H), 3.97 (s, 6H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 163.4, 157.7, 153.6, 140.8, 137.8, 132.3, 130.7, 128.6, 128.2, 114.3, 104.5, 61.0, 56.3; MS (EI, 70 eV) m/z 322.18, 307.15, 276.18, 249.13, 193.15; HRMS (ESI) calcd $C_{19}H_{19}N_2O_3$ $[M + H]^+$ m/z 323.1390, found m/z 323.1391.

*4-[4-(Hex-5-en-1-yloxy)-3,5-dimethoxyphenyl]-2-phenylpyrimidine (**3ao**).* Yellow oil: 56% yield (55 mg); IR (KBr) 3070, 2934, 2724, 1640, 1587, 1544, 1460, 1423, 1382, 1231, 1071, 1033, 834, 761, 700, 664; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80−8.79 (m, 1H), 8.56−8.55 (m, 2H), 7.52−7.51 (m, 4H), 7.46 (s, 2H), 5.90−5.82 (m, 1H), 5.06−4.95 (m, 2H), 4.09−4.06 (m, 2H), 3.97 (s, 6H), 2.16−2.11 (m, 2H), 1.85−1.78 (m, 2H), 1.65−1.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 163.6, 157.7, 153.9, 140.2, 138.8, 137.8, 132.1, 130.8, 128.6, 128.3, 114.5, 114.3, 104.7, 73.4, 56.4, 33.5, 29.6, 25.2; MS (EI, 70 eV) m/z 390.29, 308.20, 262.16; HRMS (ESI) calcd $C_{24}H_{27}N_2O_3$ $[M + H]^+$ m/z 391.2016, found m/z 391.2016.

*4-[4-(Hept-6-en-1-yloxy)-3,5-dimethoxyphenyl]-2-phenylpyrimidine (**3ap**).* Yellow oil: 51% yield (52 mg); IR (KBr) 3071, 2934, 2724, 1640, 1549, 1460, 1422, 1383, 1230, 1071, 1035, 833, 760, 700, 662; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80−8.79 (m, 1H), 8.57−8.55 (m, 2H), 7.53−7.51 (m, 4H), 7.47 (s, 2H), 5.87−5.78 (m, 1H), 5.04−4.94 (m, 2H), 4.08−4.05 (m, 2H), 3.97 (s, 6H), 2.12−2.07 (m, 2H), 1.82−1.78 (m, 2H), 1.52−1.47 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 163.6, 157.7, 153.9, 140.3, 139.0, 137.9, 132.1, 130.7, 128.6, 128.3, 114.3, 104.8, 73.6, 56.4, 33.8, 30.0, 28.7, 25.4; MS (EI, 70 eV) m/z 404.08, 308.02, 262.04, 207.04; HRMS (ESI) calcd $C_{25}H_{29}N_2O_3$ $[M + H]^+$ m/z 405.2173, found m/z 405.2176.

*4-(Furan-2-yl)-2-phenylpyrimidine (**3aq**).*[37] Yellow oil: 41% yield (23 mg); IR (KBr) 3107, 1642, 1603, 1563, 1534, 1402, 1370, 1188, 1066, 961, 851, 760, 702; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76−8.75 (m, 1H), 8.51−8.50 (m, 2H), 7.48−7.39 (m, 6H), 6.56−6.55 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 157.8, 155.6, 152.2, 145.0, 137.7, 130.7, 128.5, 128.3, 112.5, 112.4, 112.4; MS (EI, 70 eV) m/z 222.00, 194.03, 103.01, 92.01; HRMS (ESI) calcd $C_{14}H_{11}N_2O$ $[M + H]^+$ m/z 223.0866, found m/z 223.0862.

*2-Phenyl-4-(thiophen-2-yl)pyrimidine (**3ar**).* Yellow oil: 43% yield (26 mg); IR (KBr) 3072, 1563, 1426, 1386, 1345, 1068, 1036, 833, 756, 700, 626; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73−8.72 (m, 1H), 8.61−8.59 (m, 2H), 7.79−7.78 (m, 1H), 7.56−7.53 (m, 4H), 7.38−7.37 (m, 1H), 7.16−7.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 159.0, 157.6, 142.9, 137.5, 130.9, 130.2, 128.6, 128.4, 128.3, 127.5, 112.8; MS (EI, 70 eV) m/z 237.96, 134.99, 107.96, 103.00; HRMS (ESI) calcd $C_{14}H_{11}N_2S$ $[M + H]^+$ m/z 239.0637, found m/z 239.0637.

*4-(Naphthalen-1-yl)-2-phenylpyrimidine (**3as**).*[37] White solid: 53% yield (37 mg); mp 154−156 °C; IR (KBr) 3051, 1640, 1619, 1538, 1430, 1369, 1071, 1033, 849, 776, 697; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78−8.77 (m, 1H), 8.58−8.57 (m, 2H), 8.30−8.29 (m, 1H), 7.88−7.84 (m, 2H), 7.63−7.62 (m, 1H), 7.45−7.44 (m, 6H), 7.31−7.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 164.5, 157.6, 137.9, 136.3, 134.1, 131.0, 130.8, 130.4, 128.8, 128.7, 128.6, 128.2, 127.1, 126.3, 125.4, 125.4, 119.8; MS (EI, 70 eV) m/z 281.17, 178.12, 151.13, 103.08; HRMS (ESI) calcd $C_{20}H_{15}N_2$ $[M + H]^+$ m/z 283.1230, found m/z 283.1232.

*5-Methyl-2,4-diphenylpyrimidine (**3at**).*[37] White solid: 61% yield (38 mg); mp 87−88 °C; IR (KBr) 3059, 2958, 2927, 1642, 1563, 1534, 1423, 1376, 1320, 1181, 1067, 1031, 858, 752, 695; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.50−8.49 (m, 2H), 7.73 (d, J = 8.0 Hz, 2H), 7.51−7.46 (m, 6H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 162.5, 159.2, 138.5, 137.8, 130.3, 129.3, 129.1, 128.5, 128.4, 128.0, 125.6, 17.1; MS (EI, 70 eV) m/z 245.17, 142.16, 115.13, 103.10; HRMS (ESI) calcd $C_{17}H_{15}N_2$ $[M + H]^+$ m/z 247.1230, found m/z 247.1230.

*2,4,6-Triphenylpyrimidine (**3au**).*[34] White solid: 81% yield (62 mg); mp 185−186 °C; IR (KBr) 3056, 1642, 1566, 1525, 1442, 1361, 1071, 1031, 859, 735, 678; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71−8.69 (m, 2H), 8.22−8.20 (m, 4H), 7.88 (s, 1H), 7.50−7.46 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 164.5, 138.3, 137.6, 130.8, 130.7, 129.0, 128.6, 128.5, 127.4, 110.3; MS (EI, 70 eV) m/z 308.01, 205.05, 102.02; HRMS (ESI) calcd $C_{22}H_{17}N_2$ $[M + H]^+$ m/z 309.1386, found m/z 309.1386.

*4-Methyl-2,6-diphenylpyrimidine (**3av**).*[40] White solid: 58% yield (36 mg); mp 86−87 °C; IR (KBr) 3054, 2927, 1640, 1571, 1444, 1365, 1063, 1038, 963, 857, 767, 692; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 8.0 Hz, 2H), 8.15 (d, J = 8.0 Hz, 2H), 7.48−7.45 (m, 6H), 7.36 (s, 1H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 164.3, 163.7, 138.2, 137.3, 130.7, 130.5, 128.9, 128.5, 128.4, 127.2, 114.0, 24.6; MS (EI, 70 eV) m/z 246.28, 231.21, 143.17, 128.12, 102.11; HRMS (ESI) calcd $C_{17}H_{15}N_2$ $[M + H]^+$ m/z 247.1230, found m/z 247.1230.

*2-Phenylpyrimidine (**3aw**).*[41] White solid: 57% yield (22 mg); mp 36−37 °C; IR (KBr) 3041, 1641, 1561, 1419, 1366, 1319, 1180, 1068, 1034, 851, 748, 694; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78−8.77 (m, 2H), 8.45−8.44 (m, 2H), 7.48−7.47 (m, 3H), 7.14−7.13 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 157.2, 137.6, 130.8, 128.6, 128.2, 119.1; MS (EI, 70 eV) m/z 156.14, 103.09; HRMS (ESI) calcd $C_{10}H_9N_2$ $[M + H]^+$ m/z 157.0760, found m/z 157.0758.

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Synthesis of *N*-Cinnamylbenzimidamide (4). To a mixture of benzamidine (1.0 mmol), (*E*)-(3-bromoprop-1-en-1-yl)benzene (0.5 mmol), and K_2CO_3 (2.0 mmol) was added CH_3CN (3.0 mL) in a test tube equipped with a magnetic stirring bar. The mixture was stirred at room temperature for 12 h. After the reaction had been completed, the residue was directly subjected to silica gel column chromatography or purification of the mixture on a preparative TLC column to afford the desired product **4** as a colorless oil: 64% yield (0.075 g); IR (KBr) 3045, 1643, 1548, 1435, 1379, 1056, 1032, 849, 777, 699; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.53 (m, 2H), 7.32−7.16 (m, 8H), 8.56−8.52 (m, 1H), 6.31−6.27 (m, 1H), 5.43 (s, 2H), 4.05 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 137.6, 136.9, 131.5, 130.1, 128.7, 128.6, 127.5, 126.6, 126.4, 126.2, 45.1; HRMS (ESI) calcd $C_{16}H_{17}N_2$ $[M + H]^+$ m/z 237.1386, found m/z 237.1391.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00867.

^{1}H and ^{13}C spectra of all synthesized compounds (PDF)

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Notes

The authors declare no competing financial interest.

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