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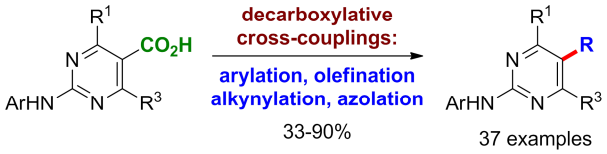

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ABSTRACT

Decarboxylative C-C cross-couplings of 2-aminopyrimidine-5-carboxylic acids under a Pd/Ag-based catalytic system opens a new platform for the introduction of diverse C5 substituents. The reaction methods proceeded efficiently with a wide range of the acids and the coupling partners of aryl iodides, alkenes, bromoalkynes, and azoles. Considering ready availability of 2-aminopyrimidine-5-carboxylic acid from the oxidative dehydrosulfurative C-N cross-coupling of the 3,4-dihydropyrimidin-1*H*-2-thiones, this reaction method unambiguously pave a shortcut to densely substituted 2-aminopyrimidine derivatives with unprecedented diversity.

1. Introduction

As evidenced in the commercialized drugs such as the hypocholesterolemic agent rosuvastatin (Crestor)[1] and the potent anticancer drug imatinib (Gleevec),[2] the 2-aminopyrimidine motifs have been recognized as important privileged substructure in drug discovery area.[3] (Figure 1). Its popularity could also be observed in the development candidates, particularly in the inhibition of protein kinases or receptors.[4] Although their growing biological importance requires facile access to highly functionalized derivatives, the traditional synthetic route towards this class of compounds usually suffers from multiple steps and the limited substrate scope.[5]

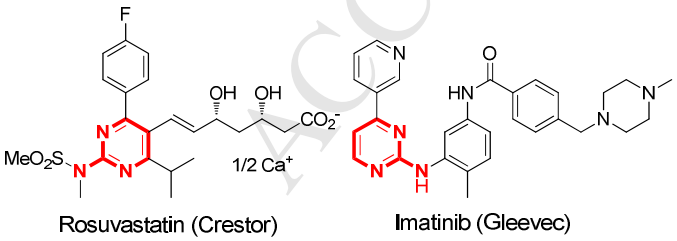
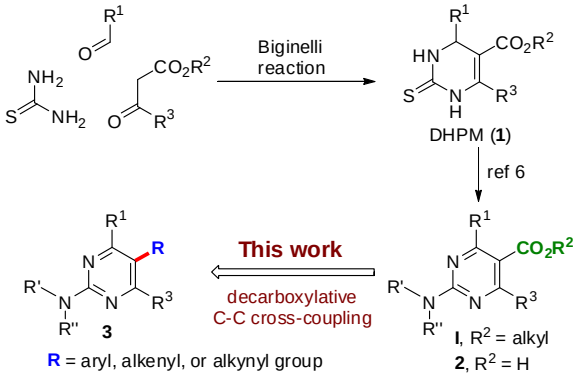


Figure 1. Structures of Rosuvastatin and imatinib.

Recently, we reported the oxidative dehydrosulfurative C-N cross-coupling of 3,4-dihydropyrimidin-1*H*-2-thiones (DHPMs) with aryl- and alkylamines to produce 2-aryl(alkyl)aminopyrimidine derivatives in a single-step under a Pd/Cu catalytic system (Scheme 1).[6] Since the well-known Biginelli three-component reaction easily produces DHPM substrates possessing diverse substituents at the C4 and C6 positions,[7] this reaction method offers preparation of pyrimidine derivatives with rapid diversification of C4 and C6 substituents, and C2 amino groups. For final derivatization of the remaining C5 position, at which substituents are usually alkoxycarbonyl groups, we focused on decarboxylative C-C cross-coupling of 2-aminopyrimidine-5-carboxylic acids **2** produced by the hydrolysis of ester **I**.



Scheme 1. Decarboxylative C-C cross-couplings of 2-aminopyrimidine-5-carboxylic acids

Transition metal-catalyzed decarboxylative cross-couplings have emerged as powerful tools to provide regiospecific carbon-carbon bond formation for target oriented synthesis.[8] Successful reactions of various aromatic carboxylates with a broad range of coupling partners have been achieved.[9,10] Five-membered heteroaromatic systems, such as oxazole-, thiazole-, pyrrole-,

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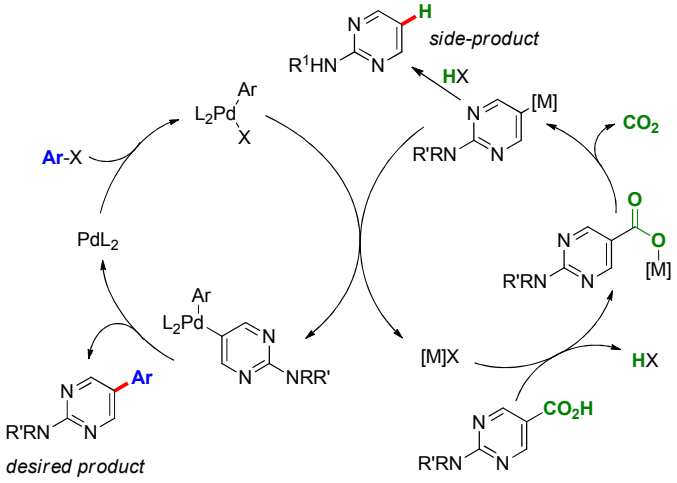
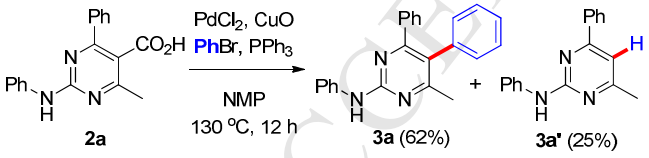
thiopene-, and furancarboxylic acids, were also suitable for the reaction.[11] However, the couplings for π-deficient heteroaromatic systems are very rare, especially for highly privileged scaffolds such as pyrimidines.[12] Herein, we report the decarboxylative C-C cross-couplings of densely substituted 2-aminopyrimidine-5-carboxylic acids with aryl iodides, alkenes, and bromoalkynes as the coupling partners under a Pd/Ag-based catalytic system. Implementation of this chemistry could offer a highly efficient route for unprecedented diversification of 2-aminopyrimidines. To achieve this regiospecific cross-coupling, it is necessary to suppress the competitive protodecarboxylation reaction (Scheme 2).



Scheme 2. Decarboxylative cross-coupling and the competitive protodecarboxylation pathways of 2-aminopyrimidinecarboxylic acid and aryl halide

2. Results and Discussion

The initial studies were decarboxylative arylation with acid **2a** and PhBr in the presence of $PdCl_2$, CuO, and PPh_3 in N-methylpyrrolidone (NMP) at 130 °C for 12 h to produce the desired decarboxylative arylation product **3a** in 62% yield, along with the protodecarboxylative product **3a'** (25%) (Scheme 3). This result paved the way for further optimization studies.



Scheme 3. Initial result of the decarboxylative arylation of **2a**

Previous work on the decarboxylative arylations of thiazole- and oxazolecarboxylic acids with aryl halides by Greaney group provided some clue to optimal conditions.[11b] Further optimization was carried out by varying the reaction parameters including the Pd source, phosphine ligand, metal source, solvent, and temperature. We obtained the desired product **3a** in 86% yield when **2a** was reacted with PhI under the reaction conditions with $PdCl_2$ (5 mol%), PPh_3 (10 mol%), Ag_2CO_3 (3 equiv), and 4 Å molecular sieves in N,N-dimethylacetamide (DMA) at 155-160 °C for 16 h. We investigated the scope of the reaction under optimal reaction conditions with various acid substrates and aryl iodides (Table 1).

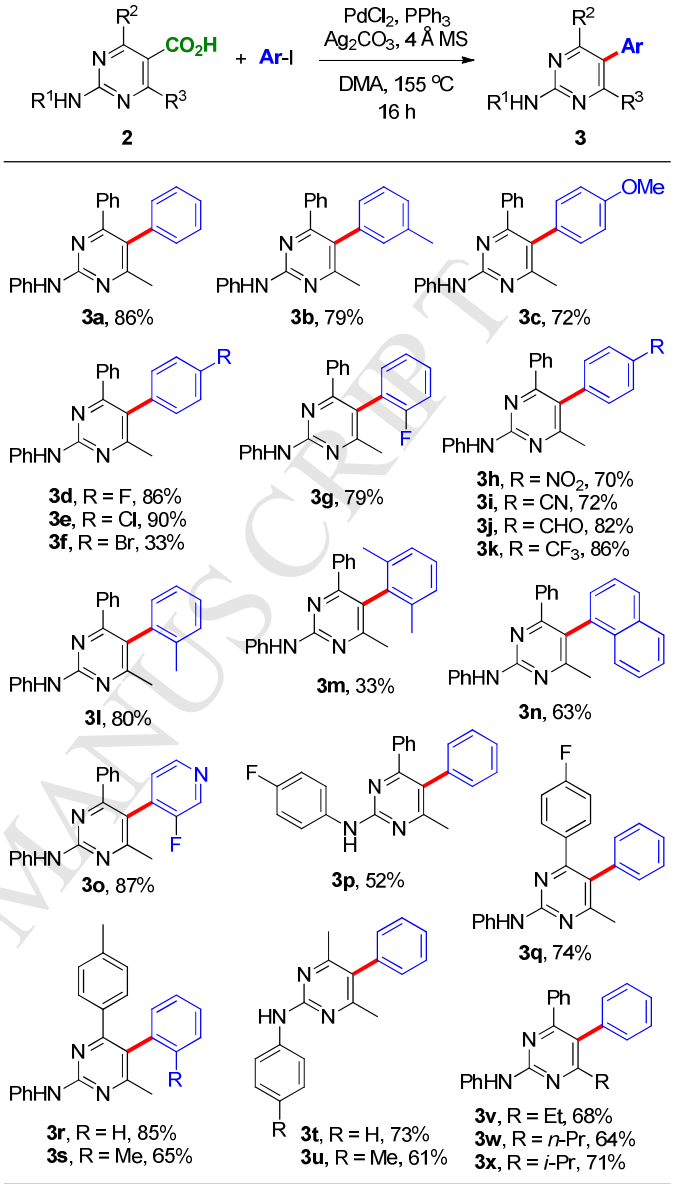


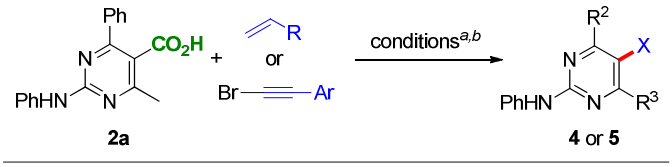
Table 1. Decarboxylative arylation[a,b]

[a]Reaction conditions; **1a**, ArI (2 equiv), $PdCl_2$ (5 mol%), PPh_3 (10 mol%), Ag_2CO_3 (3 equiv) and 4 Å MS in DMA under Ar at 155-160 °C for 16 h. [b]Isolated yields.

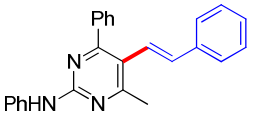
With respect to the aryl iodide, a range of functional groups on Ph and heteroaromatic ring were suitable for the reaction. First, we performed the reaction with aryl iodides containing electron-donating and withdrawing substituents to study the electronic effects. Both substituents resulted in the desired products with good yields. The m-methyl and p-methoxy groups afforded the desired products **3b** and **3c** in 79% and 72% yields, respectively. Halide groups F and Cl yielded the corresponding products **3d** (86%) and **3e** (90%), respectively, in high yields. Br afforded **3f** in low yield, which may be attributed to a competitive side-reaction. The F group at the ortho position afforded **3g** in 79% yield. Other electron-withdrawing groups, such as NO_2, CN, CHO, and CF_3 at the para position, also exhibited good yields in the production of **3h-3k**. No significant steric hindrance was observed for the o-Me group in the production of **3l** (80%), while very bulky 2,6-dimethyl groups afforded **3m** in 33% yield. Bicyclic 1-iodonaphthalene produced the desired product **3n** in

63% yield, and heterocyclic 3-fluoro-4-iodopyridine was also suitable as the reaction partner in the production of **3o** in 87% yield. We also investigated the scope of the reaction with respect to the acid substrate by varying the substituents. The reaction of the acid containing a 4-fluorophenylamino group at the C2 position with iodobenzene produced **3p** in 52% yield. When the acid possessing 4-F-C_6H_5, tolyl, or methyl group at the C4 position was reacted with iodobenzene or 1-iodo-2-methylbenzene, the corresponding products **3q**-**3u** were obtained in 61-85% yields. Acids possessing Et, *n*-Pr, and *i*-Pr groups at C6 were reacted with iodobenzene to investigate the effect of substituents at the C6 position. These substrates were also suitable for the reaction method (**3v**-**3x**, 64-71%).

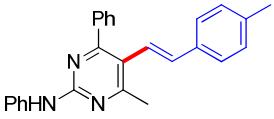
Table 2. Decarboxylative olefination and alkynylation[a-c]



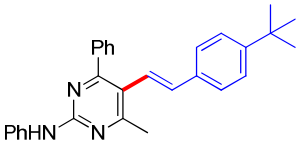
2a **4 or 5**



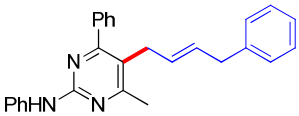
4a, 72%



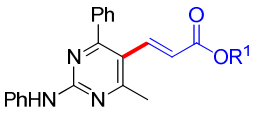
4b, 69%



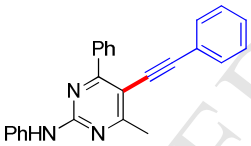
4c, 63%



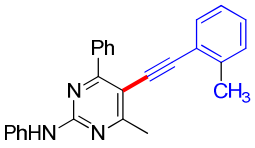
4d, 61%



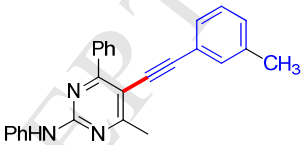
4e, R = Et, 44%
4f, R = ^{t}Bu, 41%



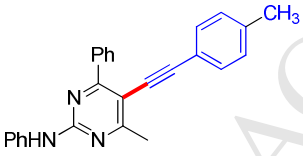
5a, 69%



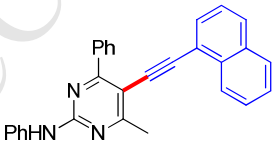
5b, 59%



5c, 65%



5d, 67%



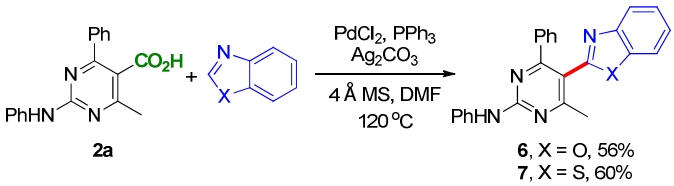
5e, 53%

[a]Reaction conditions for olefination; **1a**, olefin (2 equiv), $Pd(OAc)_2$ (20 mol%), and Ag_2CO_3 (3 equiv), 4 Å MS and DMA under Ar at 120 °C for 16 h. [b]Reaction conditions for alkynylation; **1a**, bromoalkyne (2 equiv), $PdCl_2$ (5 mol%), P(*o*-tolyl)$_3$ (10 mol%), and Ag_2CO_3 (3 equiv), 4 Å MS and DMA under Ar at 160 °C for 16 h [c]Isolated yields.

Subsequently, we studied the decarboxylative Heck reaction for olefination at the C5 position of the pyrimidine ring, which could provide facile access to rosuvastatin analogues. To our knowledge, since the first report on the decarboxylative olefination with arene carboxylic acids by Myers group in 2002,[10j] the reaction with pyrimidine substrates has not been reported yet. We performed the reaction of acid **2a** with styrene in the presence of $PdCl_2$, PPh_3, Ag_2CO_3, and 4 Å molecular sieves in DMA at 160 °C to give the desired product **4a** in 25% yield. After optimizing the reaction conditions, the desired product was obtained in 72% yield when the reaction was carried out using $Pd(OAc)_2$ with no ligand, Ag_2CO_3, and 4 Å molecular sieves in DMA at 120 °C. In this case, more amount of the Pd catalyst (20 mol%) was needed to maximize the yield compared to the arylation reaction (5 mol%). Under optimized reaction conditions, **2a** was reacted with various olefin compounds (Table 2). Styrenes possessing Me or *t*-Bu at the para position of the Ph ring produced **4b** and **4c** in 69% and 63% yields, respectively. The reaction with but-3-en-1-ylbenzene gave the non-conjugated olefin **4d** as the major product, along with the conjugated olefin **4d'** (6:1).[13] The reaction with acrylates produced esters **4e** and **4f** in 44% and 41% yields, respectively, which was lower than the yields obtained with other olefins.

We also performed decarboxylative alkynylation.[14] Initially, the terminal alkyne was selected for the reaction, but the desired alkynylated product was not produced under various reaction conditions. Among the alkyne sources for decarboxylative alkynylations, we found that bromoalkyne afforded the desired product. The reaction of acid **2a** with (bromoethynyl)benzene under the conditions with $PdCl_2$, PPh_3, and Ag_2CO_3 in N,N-dimethylformamide (DMF) at 160 °C produced **5a** in 37% yield. After optimizing the reaction conditions, the desired product was obtained in 69% yield when the reaction was performed using $PdCl_2$ (5 mol%), P(o-tolyl)$_3$ (10 mol%), Ag_2CO_3 (3.0 equiv) and 4 Å molecular sieves in DMA at 160 °C. Under these conditions, subsequent reactions were carried out with other bromoalkynes to give the corresponding decarboxylative alkynylated products. The bromoalkynes possessing ortho, meta, or para methylphenyl groups were also suitable and afforded the corresponding products **5b**-**5d**, in 59-67% yields (Table 2). We also carried out the reaction with bromaoalkynes containing bicyclic naphthyl group to produce the desired product **5e** in 53% yield. To our knowledge, the result is the first report of decarboxylative alkynylation of pyrimidine compounds.

We also investigated the decarboxylative azolation of 2-aminopyrimidine-5-carboxylic acid with azole compound for efficient synthesis of biheteroaryl pyrimidine-azole compound.[15] Relevant to this reaction, Glorius group established the intramolecular decarboxylative C-H activation of ortho-phenoxy benzoic acids for the synthesis of dibenzofurans.[9i] Crabtree and Larrosa groups reported the intermolecular cross-coupling of ortho-substituted benzoic acids with anisoles and indoles, respectively.[9g,j] Greaney group developed decarboxylative C-H arylation reaction that features the intermolecular union of two azole heteroarenes.[11c] Acid **1a** was reacted with benzoxazole in the presence of $PdCl_2$, PPh_3, Ag_2CO_3, and 4 Å molecular sieves in DMF at 120 °C to afford the desired product **6** in 56% yield. Benzothiazole was also suitable for the reaction and produce the corresponding product **7** in 60% yield.



2a

6, X = O, 56%
7, X = S, 60%

Scheme 4. Decarboxylative azolation

3. Conclusion

We developed decarboxylative C-C cross-couplings of 2-aminopyrimidine-5-carboxylic acid under a Pd/Ag-based catalytic system for facile introduction of diverse C5 substituents. The reactions proceeded efficiently with a wide range of the acids and the coupling partners of aryl iodides, alkenes, bromoalkynes, and azoles. Since the high diversity of C4 and C6 substituents, and C2 amino groups could be derived from the Biginelli reaction and our previous oxidative amination protocol, these decarboxylative couplings open a final functionalization at the C5 position to lead to densely substituted 2-aminopyrimidine derivatives, which could serve as important structures for valuable drug molecules.

4. Experimental

4.1. General information

Common solvents were purified before use. N,N-Dimethylacetamide (DMA, AcroSeal) was used as received. All reagents were reagent grade and purified where necessary. 'water' refers to distilled water. Reactions were monitored by thin layer chromatography (TLC) using Merck precoated silica gel plates. Flash column chromatography was performed over ultra pure silica gel (230-400 mesh) from Merck. Melting points were determined in opened-capillary tubes and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a AVANCE 300 MHz or 600 MHz spectrometer using residual solvent peaks as an internal standard ($CHCl_3$: δ 7.24 ppm for proton and δ 77.0 ppm for carbon). Multiplicities for ^{1}H NMR are designated as: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, m = multiplet, br = broad. Infrared spectra (IR) were recorded on JASCO FT/IR-4100 spectrometer and are reported in reciprocal centimeter (cm^{-1}). High resolution mass spectra (HRMS) were obtained on BrukermicroTOF-Q.

4.2. General procedure for decarboxylative arylation

A flame-dried tube filled with argon was charge with 2-aminopyrimidine-5-carboxylic acid **2** (0.13 mmol), $PdCl_2$ (5 mol %), PPh_3 (10 mol %), Ag_2CO_3 (0.39 mmol), ArI (0.26 mmol) and 4Å molecular sieves (100 mg) in DMA (2 mL). The resulting mixture was stirred at 155-160 ^{o}C for 16 h. After cooling to room temperature, the mixture was filtered through Celite pad and washed with EtOAc (25 mL). The filtrate was washed with water (5 mL x 2) and brine (5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (*n*-hexane/EtOAc = 10:1 v/v) to afford the corresponding product.

4.2.1. *4-methyl-N,5,6-triphenylpyrimidin-2-amine* (**3a**)[1] (86%): Pale yellow viscous oil. 1H NMR (300 MHz, CDCl3): δ 7.64 (t, J = 13.0 Hz,2H), 7.31 – 7.25 (m, 1H), 7.24 – 7.13 (m, 7H), 7.10 – 7.05 (m, 2H), 6.99 (dd, J = 12.5, 5.8 Hz, 2H), 6.90 (dd, J = 16.3, 8.9 Hz, 1H), 2.22 (s, 3H).

4.2.2. *4-methyl-N,6-diphenyl-5-(m-tolyl)pyrimidin-2-amine* (**3b**) (79%): Yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75, (d, J = 6.8 Hz, 2H), 7.45 (brs, 1H), 7.39 – 7.30 (m, 4H), 7.24-7.13 (m, 4H), 7.10 – 6.98 (m, 2H), 6.95 – 6.85 (m, 2H), 2.32 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.16, 164.53, 158.38, 140.23, 138.79, 138.13, 137.22, 131.35, 129.76, 129.03, 128.68, 128.41, 128.01, 127.84, 127.80, 124.56, 122.07, 118.80, 23.63, 21.55; IR (neat) 3056, 2926, 1552, 1518, 1443, 909, 737, 694 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{21}N_3$ $[M]^+$ 351.1735, found 351.1757.

4.2.3. *5-(4-methoxyphenyl)-4-methyl-N,6-diphenylpyrimidin-2-amine* (**3c**) (72%): Yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.9 Hz, 2H), 7.65 (brs, 1H), 7.37 – 7.29 (m, 7H), 7.15 – 7.08 (d, J = 7.3 Hz, 2H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.72 (d, *J* = 8.8 Hz, 2H), 3.76 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.87, 163.99, 160.12, 158.36, 140.26, 137.70, 131.47, 131.01, 130.76, 129.00, 128.70, 127.28, 123.94, 122.04, 118.87, 113.26, 55.32, 23.46; IR (neat) 3054, 1550, 1512, 1443, 1264, 1177, 1032, 896, 733, 704 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{21}N_3O$ $[M]^+$ 367.1685, found 367.1677.

4.2.4. *5-(4-fluorophenyl)-4-methyl-N,6-diphenylpyrimidin-2-amine* (**3d**) (86%): Yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.60 (brs, 1H), 7.45 – 7. 13 (m, 5H), , 7.10 – 6.96 (m, 5H), 6.85 (t, *J* = 7.2 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.11, 164.99, 163.74, 160.47, 158.43, 140.00, 138.50, 133.19, 133.15, 132.43, 132.33, 129.72, 129.04, 128.86, 127.97, 123.35, 122.29, 118.95, 115.82, 115.53, 23.56; IR (neat) 3414, 3276, 3058, 2924, 2853, 1600, 1552, 1509, 1443, 1383, 1296, 1264, 1223, 1158, 1093, 1029, 895, 836, 744, 693, 663, 636 cm^{-1}; HRMS (EI, m/z) calcd for $C_{23}H_{18}N_3F$ $[M]^+$ 355.1485, found 355.1477.

4.2.5. *5-(4-chlorophenyl)-4-methyl-N,6-diphenylpyrimidin-2-amine* (**3e**) (90%): Pale yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 – 7.66 (m, 2H), 7.51 (brs, 1H), 7.37 – 7.28 (m, 5H), 7.42 – 7.14 (m, 9H), 7.07 – 6.99 (m, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.78, 165.01, 158.18, 139.76, 138.23, 135.66, 133.45, 132.11, 129.73, 129.07, 128.91, 128.07, 127.93, 123.15, 122.49, 119.06, 23.55; IR (neat) 3409, 3274, 3057, 2924, 1596, 1551, 1518, 1496, 1444, 1265, 1090, 828, 750, 693 cm^{-1}; HRMS (EI, m/z) calcd for $C_{23}H_{18}N_3Cl$ $[M]^+$ 371.1189, found 371.1167.

4.2.6. *5-(4-bromophenyl)-4-methyl-N,6-diphenylpyrimidin-2-amine* (**3f**) (33%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, J = 7.9 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 7.36 – 7.29 (m, 4H), 7.29 – 7.21 (m, 3H), , 7.03 (t, *J* = 7.3, 1H), 6.98 (d, J = 7.3 Hz, 2H), 2.31 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.96, 164.81, 158.54, 139.95, 138.42, 136.39, 132.46, 131.81, 129.71, 129.07, 128.92, 128.06, 123.22, 122.33, 121.50, 118.93, 23.72; IR (neat) 3053, 2305, 1552, 1518, 1444, 1264, 896, 733, 704 cm^{-1}; HRMS (EI, m/z) calcd for $C_{23}H_{18}N_3Br$ $[M]^+$ 415.0684, found 415.0667.

4.2.7. *5-(2-fluorophenyl)-4-methyl-N,6-diphenylpyrimidin-2-amine* (**3g**) (79%): Yellow viscous oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (brs, 1H), 7.77 (d, J = 7.6 Hz, 2H), 7.40 – 7.24 (m, 8H), 7.12 – 6.95 (m, 4H), 2.34 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.30, 167.29, 166.04, 161.12, 159.50, 158.27, 139.66, 138.18, 132.56, 132.54, 130.04, 129.99, 129.22, 129.16, 129.04, 128.03, 124.66, 124.46, 124.43, 122.62, 119.29, 117.87, 115.94, 115.79, 22.74; IR (neat) 3059, 2925, 1554, 1520, 1445, 1384, 1255, 755, 694 cm^{-1}; HRMS (EI, m/z) calcd for $C_{23}H_{18}N_3F$ $[M]^+$ 355.1485, found 355.1473.

4.2.8. *4-methyl-5-(4-nitrophenyl)-N,6-diphenylpyrimidin-2-amine* (**3h**) (70%): Yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.46 (m, 1H), 7.39 – 7.17 (m, 9H), , 7.15 – 7.11 (m, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.38, 165.25, 158.81, 147.03, 144.83, 139.72, 137.90, 131.88, 129.65, 129.31, 129.07, 128.23, 128.18, 123.78, 122.64, 119.20, 23.38; IR (neat) 3058, 2928, 1596, 1551, 1517, 1444, 1344, 1265, 855, 750, 701

cm^{-1}; HRMS (EI, m/z) calcd for $C_{23}H_{18}N_4O_2$ $[M]^+$ 382.1430, found 382.1417.

4.2.9. *4-(4-methyl-6-phenyl-2-(phenylamino)pyrimidin-5-yl)benzonitrile* (**3i**) (72%): White solid; m.p. 213-214 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 7.44 (brs, 1H), 7.35 (t, J = 8.0 Hz, 2H), 7.29 – 7.19 (m, 7H), 7.05 (t, J = 7.9 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.47, 165.03, 158.71, 142.76, 139.65, 137.97, 132.32, 131.70, 129.64, 129.23, 129.10, 128.19, 122.70, 122.61, 119.08, 118.79, 111.20, 23.66; IR (neat) 3325, 3054, 2230, 1550, 1518, 1444, 1264, 896, 837, 732, 703 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{18}N_4$ $[M]^+$ 362.1531, found 362.1547.

4.2.10. *4-(4-methyl-6-phenyl-2-(phenylamino)pyrimidin-5-yl)benzaldehyde* (**3j**) (82%): Colorless viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.81 (dd, *J* = 13.5, 7.1 Hz, 4H), 7.43 – 7.15 (m, 9H), 7.04 (t, *J* = 7.4 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.91, 166.55, 165.02, 158.69, 144.25, 139.87, 138.17, 135.20, 131.64, 129.89, 129.71, 129.11, 129.06, 128.08, 128.05, 122.47, 119.10, 23.46; IR (neat) 3054, 2305, 1702, 1553, 1519, 1444, 1264, 896, 732, 704 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{19}N_3O$ $[M]^+$ 365.1528, found 365.1539.

4.2.11. *4-methyl-N,6-diphenyl-5-(4-(trifluoromethyl)phenyl)pyrimidin-2-amine* (**3k**) (86%): Pale yellow viscous oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.5 (d, J = 8.2 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.52 (brs, 1H), 7.35 (t, J = 8.1 Hz, 2H), 7.31 – 7.27 (m, 3H), 7.22 (t, *J* = 8.5 Hz, 4H), 7.04 (tt, *J* = 7.3, 1.2 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.78, 165.00, 158.66, 141.41, 139.86, 138.20, 131.24, 129.69, 129.42, 129.08, 129.07, 128.09, 125.57, 125.54, 125.52, 125.49, 123.31, 123.07, 122.46, 119.04, 23.62; IR (neat) 3406, 2925, 1549, 1320, 1160, 1067, 841, 759, 691 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{18}N_3F_3$ $[M]^+$ 405.1453, found 405.1457.

4.2.12. *4-methyl-N,6-diphenyl-5-(o-tolyl)pyrimidin-2-amine* (**3l**) (80%): Yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (m, 2H), 7.49 – 7.21 (m, 7H), 7.29 – 7.21 (m, 3H), 7.11 (t, J = 8.2 Hz, 1H) 7.04 (s, 1H), 2.40 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.69, 163.97, 161.99, 144.58, 143.92, 137.48, 136.90, 131.11, 130.44, 129.69, 128.73, 128.47, 127.06, 127.04, 126.72, 125.56, 124.01, 107.63, 24.72, 18.62; IR (neat) 3061, 2922, 1571, 1544, 1493, 1460, 1412, 1373, 1347, 767, 721, 693 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{21}N_3$ $[M]^+$ 351.1735, found 351.1745.

4.2.13. *5-(2,6-dimethylphenyl)-4-methyl-N,6-diphenylpyrimidin-2-amine* (**3m**) (33%): Yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.81 (m, 2H), 7.41 – 7.33 (m, 5H), 7.30 (s, 1H), 7.28 (s, 1H), 7.22 – 7.10 (m, 3H), 7.07 – 7.00 (m, 2H), 2.40 (s, 3H), 2.08 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.71, 164.12, 161.37, 143.05, 142.25, 137.54, 137.23, 130.42, 128.73, 128.69, 128.28, 127.13, 127.07, 123.58, 123.17, 107.72, 24.72, 18.70; IR (neat) 3061, 2922, 2853, 1571, 1544, 1494, 1410, 1372, 1347, 1029, 767, 741, 692 cm^{-1}; HRMS (EI, m/z) calcd for $C_{25}H_{23}N_3$ $[M]^+$ 365.1892, found 365.1890.

4.2.14. *4-methyl-5-(naphthalen-1-yl)-N,6-diphenylpyrimidin-2-amine* (**3n**) (63%): Yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (t, *J* = 7.6 Hz, 2H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.73 – 7.68 (m, 2H), 7.57 – 7.49 (m, 2H), 7.49 – 7.42 (m, 4H), 7.38 – 7.36 (m, 1H), 7.36 – 7.29 (m, 4H), 7.14 – 7.08 (m, 1H), 7.04 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.70, 163.96, 162.85, 145.36, 142.10, 137.44, 134.95, 131.81, 130.37, 128.66, 128.57, 128.47, 127.24, 127.03, 126.47, 126.29, 125.97, 125.55, 124.22, 124.13, 107.90, 24.70; IR (neat) 3058, 2925, 1572, 1544, 1494, 1412, 1372, 1347, 1027, 768, 738, 893, 639 cm^{-1}; HRMS (EI, m/z) calcd for $C_{27}H_{21}N_3$ $[M]^+$ 387.1735, found 387.1737.

4.2.15. *5-(3-fluoropyridin-4-yl)-4-methyl-N,6-diphenylpyrimidin-2-amine* (**3o**) (87%): Yellow viscous oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (d, *J* = 5.1 Hz, 1H), 7.87 (brs, 1H), 7.78 – 7.70 (d, J = 7.5 Hz, 2H), 7.41 – 7.27 (m, 6H), 7.07 (t, *J* = 8.5 Hz, 1H), 6.94 (dt, *J* = 5.1, 1.7 Hz, 1H), 6.72 (d, *J* = 1.7 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.96, 165.34, 164.78, 163.19, 158.48, 151.51, 147.94, 147.84, 139.32, 137.37, 129.68, 129.53, 129.11, 128.37, 123.80, 123.77, 122.97, 120.76, 120.74, 119.41, 111.78, 111.54, 23.26; IR (neat) 3281, 3059, 2927, 1602, 1552, 1518, 1444, 1405, 1295, 1247, 1189, 892, 748, 695 cm^{-1}; HRMS (EI, m/z) calcd for $C_{22}H_{17}N_4F$ $[M]^+$ 356.1437, found 356.1451.

4.2.16. *N-(4-fluorophenyl)-4-methyl-5,6-diphenylpyrimidin-2-amine* (**3p**) (52%): Pale yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (brs, 1H), 7.73 – 7.67 (dd, J = 8.5 Hz, 1.2 Hz, 2H), 7.35 – 7.27 (m, 5H), 7.24 – 7.17 (m, 3H), 7.08 – 6.99 (m, 4H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.17, 164.75, 158.39, 156.73, 138.63, 137.24, 136.22, 130.76, 130.48, 129.73, 128.78, 128.59, 127.86, 127.71, 127.33, 124.48, 120.52, 120.42, 115.68, 115.38, 23.55; IR (neat) 3416, 3275, 3058, 2925, 1554, 1505, 1413, 1218, 831, 739, 700 cm^{-1}; HRMS (EI, m/z) calcd for $C_{23}H_{18}N_3F$ $[M]^+$ 355.1485, found 355.1487.

4.2.17. *4-(4-fluorophenyl)-6-methyl-N,5-diphenylpyrimidin-2-amine* (**3q**) (74%): Pale yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (brs, 1H), 7.75 (d, *J* = 8.5 Hz, 2H), 7.36 – 7.31 (m, 6H), 7.13 – 7.07 (m, 3H), 6.89 (t, *J* = 8.6 Hz, 3H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.39, 163.43, 161.35, 158.49, 140.08, 137.28, 134.81, 131.84, 131.73, 130.72, 129.06, 128.74, 127.44, 124.29, 122.24, 118.88, 115.03, 114.75, 23.71; IR (neat) 3053, 2253, 1554, 1520, 1443, 1265, 905, 726 cm^{-1}; HRMS (EI, m/z) calcd for $C_{23}H_{18}N_3F$ $[M]^+$ 355.1485, found 355.1475.

4.2.18. *4-methyl-N,5-diphenyl-6-(p-tolyl)pyrimidin-2-amine* (**3r**) (85%): Pale yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.51 – 7.19 (m, 8H), 7.14 – 7.08 (m, 2H), 7.00 (d, *J* = 7.7 Hz, 3H), 2.29 (d, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.99, 164.52, 158.45, 140.25, 138.78, 137.61, 135.84, 130.77, 129.79, 129.01, 128.60, 128.58, 127.23, 124.27, 122.04, 118.83, 23.60, 21.40; IR (neat) 3403, 3275, 3056, 2922, 1549, 1518, 1442, 1423, 1264, 800, 746, 702 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{21}N_3$ $[M]^+$ 351.1735, found 351.1754.

4.2.19. *4-methyl-N-phenyl-5-(o-tolyl)-6-(p-tolyl)pyrimidin-2-amine* (**3s**) (65%): Pale yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.45 – 7.27 (m, 9H), 7.19 – 7.12 (m, 1H), 7.08 (s, 1H), 2.44 (s, 3H), 2.43 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.48, 163.92, 161.95, 144.64, 144.00, 140.68, 136.93, 134.72, 131.07, 129.70, 129.46, 128.43, 127.02, 126.96, 126.65, 125.50, 123.88, 107.30, 24.74, 21.52, 18.62; IR (neat) 3404, 3276, 3060, 2922, 1570, 1547, 1518, 1490, 1442, 1412, 1360, 1264, 800, 726, 700 cm^{-1}; HRMS (EI, m/z) calcd for $C_{25}H_{23}N_3$ $[M]^+$ 365.1892, found 365.1887.

4.2.20. *4,6-dimethyl-N,5-diphenylpyrimidin-2-amine* (**3t**) (73%): Pale yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 – 7.69 (m, 3H), 7.49 – 7.30 (m, 5H), 7.21 – 7.14 (m, 2H), 7.02 (t, *J* = 7.4 Hz, 1H), 2.20 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.50, 157.84, 139.98, 137.14, 129.78, 129.00, 128.95, 127.70, 125.58, 122.28, 119.04, 23.03; IR (neat) 3277, 3056, 2925, 1565, 1520,

1441, 1261, 744, 702 cm^{-1}; HRMS (EI, m/z) calcd for $C_{18}H_{17}N_3$ $[M]^+$ 275.1422, found 275.1437.

4.2.21. *4,6-dimethyl-5-phenyl-N-(p-tolyl)pyrimidin-2-amine* (**3u**) (61%): Pale yellow viscous oil. ^1H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.4 Hz, 2H), 7.46 – 7.35 (m, 4H), 7.17 (d, J = 8.3 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 2.32 (s, 3H), 2.17 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.43, 158.23, 137.50, 137.45, 131.68, 129.83, 129.48, 128.89, 127.58, 125.35, 119.19, 23.11, 20.93; IR (neat) 3275, 3056, 2925, 1565, 1520, 1441, 1378, 1261, 744, 702 cm^{-1}; HRMS (EI, m/z) calcd for $C_{19}H_{19}N_3$ $[M]^+$ 289.1579, found 289.1570.

4.2.22. *4-ethyl-N,5,6-triphenylpyrimidin-2-amine* (**3v**) (68%): Orange viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.74 (m, 2H), 7.41 – 7.27 (m, 8H), 7.24 – 7.15 (m, 3H), 7.13 – 7.08 (m, 2H), 7.02 (t, *J* = 7.4 Hz, 1H), 2.61 (q, *J* = 7.5 Hz, 2H), 1.23 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.45, 164.88, 158.78, 140.31, 138.87, 137.19, 130.92, 129.71, 129.01, 128.60, 128.47, 127.82, 127.25, 122.00, 118.77, 28.94, 13.01; IR (neat) 3058, 2930, 1550, 1517, 1443, 1420, 744, 700 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{21}N_3$ $[M]^+$ 351.1735, found 351.1745.

4.2.23. *N,4,5-triphenyl-6-propylpyrimidin-2-amine* (**3w**) (64%): Pale yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.36 – 7.16 (m, 9H), 7.15 – 7.07 (m, 2H), 7.06 – 6.88 (m, 3H), 2.49 (td, *J* = 7.7, 2.5 Hz, 2H), 1.65 (qd, *J* = 7.5, 2.4 Hz, 2H), 0.81 (td, *J* = 7.4, 2.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.35, 164.94, 158.62, 140.26, 138.91, 137.20, 130.99, 129.70, 129.02, 128.60, 128.43, 127.81, 127.23, 124.41, 122.01, 118.74, 37.51, 22.05, 14.23; IR (neat) 3406, 3058, 2962, 2870, 1548, 1517, 1443, 1420, 743, 700 cm^{-1}; HRMS (EI, m/z) calcd for $C_{25}H_{23}N_3$ $[M]^+$ 365.1892, found 365.1887.

4.2.24. *4-isopropyl-N,5,6-triphenylpyrimidin-2-amine* (**3x**) (71%): Pale yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, J = 8.2 Hz, 2H), 7.43 – 7.22 (m, 7H), 7.15 – 7.08 (m, 2H), 7.03 (ddt, *J* = 8.5, 7.3, 1.2 Hz, 1H), 6.93 – 6.83 (m, 3H), 3.04 (heptet, *J* = 6.7 Hz, 1H), 1.24 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.78, 165.55, 158.94, 140.53, 138.72, 137.42, 137.15, 130.99, 130.15, 128.96, 128.27, 127.49, 127.07, 123.45, 121.74, 118.59, 32.05, 22.18; IR (neat) 2962, 1550, 1516, 1442, 749, 703 cm^{-1}; HRMS (EI, m/z) calcd for $C_{25}H_{23}N_3$ $[M]^+$ 365.1892, found 365.1880.

4.3. General procedure for decarboxylative olefination

A flame-dried tube filled with argon was charge with 2-aminopyrimidine-5-carboxylic acid **2** (0.13 mmol), $Pd(OAc)_2$ (20 mol %), Ag_2CO_3 (0.39 mmol), alkene (0.20 mmol) and 4Å molecular sieves (100 mg) in DMA (2 mL). The resulting mixture was stirred at 120 ^oC for 16 h. After cooling to room temperature, the mixture was filtered through Celite pad and washed with EtOAc (25 mL). The filtrate was washed with water (5 mL x 2) and brine (5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (*n*-hexane/EtOAc = 10:1) to afford the corresponding product.

4.3.1. *(E)-4-methyl-N,6-diphenyl-5-styrylpyrimidin-2-amine* (**4a**) (72%): Yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 – 7.66 (m, 4H), 7.48 (brs, 1H) 7.45 – 7.38 (m, 4H), 7.37 – 7.26 (m, 6H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 16.6 Hz, 1H), 6.53 (d, *J* = 16.6 Hz, 1H), 2.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.60, 165.43, 157.45, 139.99, 138.96, 137.36, 134.44, 129.82, 129.32, 129.05, 128.84, 128.32, 127.85, 126.35, 123.79, 122.22, 120.10, 118.85, 24.10; IR (neat) 3285, 3057, 2922, 2851, 1638, 1596, 1548, 1518, 1496, 1444, 1380, 1264, 1075, 1030, 968, 895, 749, 699 cm^{-1}; HRMS (EI, m/z) calcd for $C_{25}H_{21}N_3$ $[M]^+$ 363.1735, found 363.1747.

4.3.2. *(E)-4-methyl-5-(4-methylstyryl)-N,6-diphenylpyrimidin-2-amine* (**4b**) (69%): Yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 – 7.70 (m, 5H), 7.49 – 7.44 (m, 3H), 7.37 (t, *J* = 7.9 Hz, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 16.6 Hz, 1H), 6.53 (d, *J* = 16.6 Hz, 1H), 2.68 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.54, 165.33, 157.39, 140.04, 138.98, 137.81, 134.60, 134.43, 129.83, 129.53, 129.26, 129.02, 128.28, 126.26, 122.72, 122.18, 120.27, 118.86, 23.97, 21.36; IR (neat) 3403, 3277, 3026, 2921, 1596, 1546, 1515, 1497, 1443, 1376, 1250, 970, 795, 751, 700 cm^{-1}; HRMS (EI, m/z) calcd for $C_{26}H_{23}N_3$ $[M]^+$ 377.1892, found 377.1900.

4.3.3. *(E)-5-(4-(tert-butyl)styryl)-4-methyl-N,6-diphenylpyrimidin-2-amine* (**4c**) (63%): Yellow viscous oil. ^1H NMR (600 MHz, $CDCl_3$) δ 7.76 – 7.72 (m, 2H), 7.71 – 7.68 (m, 2H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.43 (dd, *J* = 5.3, 2.0 Hz, 3H), 7.37 – 7.31 (m, 4H), 7.30 – 7.27 (m, 2H), 7.02 (td, *J* = 7.4, 1.1 Hz, 1H), 6.89 (d, *J* = 16.6 Hz, 1H), 6.51 (d, *J* = 16.6 Hz, 1H), 2.63 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.60, 165.32, 157.41, 151.07, 140.05, 139.04, 134.62, 134.27, 129.81, 129.25, 129.04, 128.30, 127.93, 126.11, 125.78, 123.00, 122.18, 118.85, 34.77, 31.42, 24.08; IR (neat) 3278, 3056, 2960, 2865, 1600, 1547, 1517, 1497, 1444, 1363, 1250, 970, 751, 700 cm^{-1}; HRMS (EI, m/z) calcd for $C_{29}H_{29}N_3$ $[M]^+$ 419.2361, found 419.2349.

4.3.4. *(E)-4-methyl-N,6-diphenyl-5-(4-phenylbut-2-en-1-yl)pyrimidin-2-amine* (**4d**) (61%): Yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (m, 3H), 7.60 – 7.48 (m, 2H), 7.47 – 7.35 (m, 4H), 7.35 – 7.22 (m, 4H), 7.15 (d, *J* = 7.3 Hz, 2H), 5.72 – 5.56 (m, 1H), 5.53 – 5.35 (m, 1H), 3.37 (d, *J* = 6.8 Hz, 2H), 3.29 (d, *J* = 4.5 Hz, 2H), 2.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.45, 168.17, 166.66, 140.35, 140.14, 130.67, 128.92, 128.78, 128.43, 128.57, 128.39, 128.13, 126.06, 123.78, 121.74, 119.20, 118.46, 39.02, 31.17, 22.41; IR (neat) 3286, 3027, 2921, 2851, 1554, 1522, 1496, 1443, 1381, 1252, 746, 699 cm^{-1}; HRMS (EI, m/z) calcd for $C_{27}H_{25}N_3$ $[M]^+$ 391.2048, found 391.2054.

4.3.5. *(E)-ethyl 3-(4-methyl-6-phenyl-2-(phenylamino)pyrimidin-5-yl)acrylate* (**4e**) (44%): Yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$) 7.75 – 7.68 (m, 3H), 7.64 (s, 1H), 7.57 (m, 2H), 7.49 – 7.45 (m, 3H), 7.34 (t, *J* = 8.4, 2H), 7.09 – 7.02 (t, *J* = 8.4 Hz, 1H), 5.94 (d, *J* = 16.3 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 2.64 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.53, 167.26, 166.72, 158.00, 140.17, 139.43, 138.22, 134.43, 129.86, 129.67, 129.08, 128.54, 122.80, 119.26, 117.39, 60.66, 24.52, 14.41; IR (neat) 3339, 2926, 1710, 1598, 1546, 1518, 1445, 1377, 1290, 1252, 1178, 1034, 985, 750, 701 cm^{-1}; HRMS (EI, m/z) calcd for $C_{22}H_{21}N_3O_2$ $[M]^+$ 359.1634, found 359.1637.

4.3.6. *(E)-tert-butyl 3-(4-methyl-6-phenyl-2-(phenylamino)pyrimidin-5-yl)acrylate* (**4f**) (41%): Yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.72 – 7.69 (d, *J* = 7.5 Hz, 2H), 7.60 – 7.54 (m, 3H), 7.48 – 7.43 (m, 4H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.04 (t, *J* = 7.4, 1H), 5.88 (d, *J* = 16.3 Hz, 1H), 2.63 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.50, 167.21, 166.03, 157.96, 139.53, 139.10, 138.30, 129.76, 129.68, 129.08, 128.45, 124.53, 122.71, 119.19, 117.52, 80.68, 28.32, 24.67; IR (neat) 3326, 2976, 2929, 1704, 1546, 1518, 1497, 1445, 1367,

1290, 1251, 1150, 741, 700 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{25}N_3O_2$ $[M]^+$ 387.1947, found 387.1936.

4.4. General procedure for decarboxylative alkynylation

A flame-dried tube filled with argon was charge with 2-aminopyrimidine-5-carboxylic acid **2** (0.13 mmol), $PdCl_2$ (5 mol %), P(*o*-tolyl)$_3$ (10 mol %), Ag_2CO_3 (0.39 mmol), bromoalkyne (0.26 mmol) and 4Å molecular sieves (100 mg) in DMA (2 mL). The resulting mixture was stirred at 160 ^oC for 16 h. After cooling to room temperature, the mixture was filtered through Celite pad and washed with EtOAc (25 mL). The filtrate was washed with water (5 mL x 2) and brine (5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (*n*-hexane/EtOAc = 10:1) to afford the corresponding product.

4.4.1. *4-methyl-N,6-diphenyl-5-(phenylethynyl)pyrimidin-2-amine* (**5a**) (69%): Brown viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ 8.12 (m, 2H), 7.67 (dd, *J* = 8.6, 4.7 Hz, 2H), 7.50 – 7.49 (m, 4H), 7.47 (brs, 1H), 7.43 – 7.36 (m, 2H), 7.37 – 7.29 (m, 3H), 7.04 (t, *J* = 8.7 Hz, 2H), 2.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 156.9, 139.3, 137.7, 130.9, 130.2, 129.4, 129.0, 128.4, 128.3, 128.0, 123.4, 122.7, 119.2, 98.4, 85.2, 23.7; IR (neat) 3057, 2924, 1597, 1550, 1516, 1494, 1445, 754, 691 cm^{-1}; HRMS (EI, m/z) calcd for $C_{25}H_{19}N_3$ $[M]^+$ 361.1579, found 361.1583.

4.4.2. *4-methyl-N,6-diphenyl-5-(o-tolylethynyl)pyrimidin-2-amine* (**5b**) (59%): Yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ 8.12 (m, 2H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.53 (brs, 1H), 7.51 – 7.46 (m, 3H), 7.35 (t, *J* = 8.5 Hz, 4H), 7.22 – 7.17 (m, 2H), 7.08 – 7.02 (m, 1H), 2.73 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 166.8, 157.2, 139.8, 139.6, 138.1, 131.6, 130.1, 129.7, 129.5, 129.1, 128.4, 128.1, 125.8, 123.4, 122.7, 119.3, 106.7, 97.7, 89.1, 24.2, 21.0; IR (neat) 3405, 3278, 3058, 2922, 2853, 1546, 1514, 1494, 1444, 752, 692 cm^{-1}; HRMS (EI, m/z) calcd for $C_{26}H_{21}N_3$ $[M]^+$ 375.1735, found 375.1747.

4.4.3. *4-methyl-N,6-diphenyl-5-(m-tolylethynyl)pyrimidin-2-amine* (**5c**) (65%): Yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$ δ 8.15 (dd, *J* = 7.9, 1.8 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.54 – 7.49 (m, 3H), 7.35 (t, *J* = 8.5 Hz, 3H), 7.22 (d, *J* = 8.5 Hz, 3H), 7.13 (d, *J* = 8.4 Hz, 1H), 7.06 (t, J = 7.4 Hz, 1H), 2.73 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 166.8, 156.6, 139.3, 138.5, 137.8, 130.9, 130.2, 129.4, 129.2, 128.9, 128.0, 122.7, 120.3, 119.3, 106.4, 98.7, 84.4, 23.5, 21.5; IR (neat) 3057, 2922, 2853, 1549, 1516, 1496, 1445, 783, 751, 691 cm^{-1}; HRMS (EI, m/z) calcd for $C_{26}H_{21}N_3$ $[M]^+$ 375.1735, found 375.1740.

4.4.4. *4-methyl-N,6-diphenyl-5-(p-tolylethynyl)pyrimidin-2-amine* (**5d**) (67%): Yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$) 8.15 (s, 2H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.51 (s, 3H), 7.43 – 7.21 (m, 4H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.09 – 6.94 (m, 1H), 2.73 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 166.8, 156.6, 139.3, 138.5, 137.8, 130.9, 130.2, 129.4, 129.2, 128.9, 128.0, 122.7, 120.3, 119.3, 106.4, 98.7, 84.4, 23.5, 21.5; IR (neat) 3284, 3056, 2922, 1550, 1513, 1497, 1445, 816, 753, 692 cm^{-1}; HRMS (EI, m/z) calcd for $C_{26}H_{21}N_3$ $[M]^+$ 375. 1735, found 375.1751.

4.4.5. *4-methyl-5-(naphthalen-1-ylethynyl)-N,6-diphenylpyrimidin-2-amine* (**5e**) (53%): Yellow viscous oil. ^1H NMR (600 MHz, $CDCl_3$) δ 8.21 – 8.12 (m, 2H), 8.07 (d, *J* = 7.9 Hz, 1H), 7.83 (t, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 7.9 Hz, 2H), 7.63 (d, *J* = 7.1 Hz, 1H), 7.57 – 7.31 (m, 9H), 7.07 (t, *J* = 7.3 Hz, 1H), 2.85 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.2, 167.2, 157.1, 139.4, 138.2, 133.4, 133.1, 130.3, 130.1, 129.5, 129.1, 128.8, 128.4, 128.3, 126.9, 126.6, 126.3, 125.4, 122.9, 121.3, 119.4, 106.8, 97.1, 90.0, 24.3; IR (neat) 3411, 3054, 1548, 1515, 1445, 1264, 734, 703 cm^{-1}; HRMS (EI, m/z) calcd for $C_{29}H_{21}N_3$ $[M]^+$ 411.1735, found 411.1749.

4.5. Decarboxylative azolation

A flame-dried tube filled with argon was charge with acid **2a** (0.13 mmol), $PdCl_2$ (5 mol %), PPh_3 (10 mol %), Ag_2CO_3 (0.39 mmol), benzoxazole (0.13 mmol) and 4Å molecular sieves (100 mg) in DMF (2 mL). The resulting mixture was stirred at 120 ^oC for 18 h. After cooling to room temperature, the mixture was filtered through Celite pad and washed with EtOAc (25 mL). The filtrate was washed with water (5 mL x 2) and brine (5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (*n*-hexane/EtOAc = 20:1 v/v) to afford the corresponding product.

4.5.1. *5-(benzo[d]oxazol-2-yl)-4-methyl-N,6-diphenylpyrimidin-2-amine* (**6**) (56%): yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ) δ 7.76 (d, *J* = 7.4 Hz, 3H), 7.55 - 7.16 (m, 11H), 7.08 (t, *J* = 7.2 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.47, 167.31, 164.28, 159.34, 141.62, 139.18, 129.92, 129.12, 128.53, 125.44, 124.61, 123.14, 120.34, 119.61, 110.80, 23.41; IR (neat) 3275, 3059, 2927, 1548, 1521, 1445, 1250, 743, 692 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{18}N_4O$ $[M]^+$ 378.1481, found 378.1487.

4.5.2. *5-(benzo[d]thiazol-2-yl)-4-methyl-N,6-diphenylpyrimidin-2-amine* (**7**) (60%): Yellow viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.2, 1H) 7.88 - 7.69 (m 3H), 7.64 - 7.44 (m, 5H), 7.41 – 7.23 (m, 5H), 7.06 (t, J = 7.4 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.54, 165.97, 165.20, 159.22, 153.28, 139.46, 137.99, 136.83, 129.66, 129.39, 129.09, 128.36, 126.26, 125.46, 123.59, 122.86, 121.67, 119.38, 117.29, 23.40; IR (neat) 3270, 3059, 2922, 1551, 1524, 1444, 758, 731, 695 cm^{-1}; HRMS (EI, m/z) calcd for $C_{24}H_{18}N_4S$ $[M]^+$ 394.1252, found 394.1265.

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Supplementary data

Supplementary data related with this article can be found at http://

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