JOC The Journal of Organic Chemistry

Note

Base-Mediated Three-Component Tandem Reactions for the Synthesis of Multi-Substituted Pyrimidines

Dongqing Liu, Wei Guo, Wanqing Wu, and Huanfeng Jiang

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b02113 • Publication Date (Web): 21 Nov 2017

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Base-Mediated Three-Component Tandem Reactions for the Synthesis of Multi-Substituted Pyrimidines

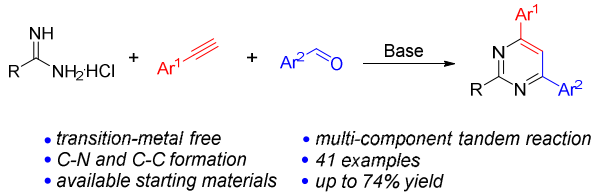
Dongqing Liu,[a,c] Wei Guo,[a,b,c] Wanqing Wu,[a,*] Huanfeng Jiang[a,*]

[a] Key Laboratory of Functional Molecular Engineering of Guangdong Province, School of Chemistry and Chemical Engineering, Key Laboratory of Functional Molecular Engineering of Guangdong Province, South China University of Technology, Guangzhou 510640, China

Fax: (+86) 20-8711-2906; E-mail: cewuwq@scut.edu.cn, jianghf@scut.edu.cn

[b] Key Laboratory of Organo-pharmaceutical Chemistry of Jiangxi Province, Gannan Normal University, Ganzhou 341000, China

[c] D. Liu and W. Guo contributed equally.

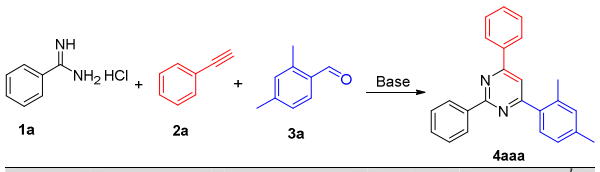


ABSTRACT: Base mediated three-component tandem reaction for the synthesis of multi-substituted pyrimidines from amidines, aryl alkynes and aldehydes in a one-pot manner has been developed. This transformation features transition-metal free, high efficiency, available starting materials and environmentally friendly advantage.

Pyrimidines represent one of the most important heterocycles in biologically active molecules, naturally products, and functional materials.[1] Notably, much attention has been directed toward the pyrimidines with biological activities, including anti-cancer, anti-inflammatory, anti-mycobacterial, antibacterial and antimalarial.[2] In addition, pyrimidines can be used as potential candidates for photophysical materials, especially light emitting devices.[3] Although a number of methods have been developed for the preparation of pyrimidines,[4] most of them are mainly confined to expensive and moisture sensitive reagents,[5] use multistep reactions,[6] microwave irradiation,[7] transition metal catalysts[8] and unavailable starting materials.[9] Despite an appealing synthetic strategy, the design and development of novel domino reactions for the acquisition of pyrimidines from easily available starting materials under green conditions continues to be a challenge.[10]

Sequential tandem one-pot reactions with two or more components have emerged as one of the powerful tools in organic synthesis for the construction of the diversity and complexity of the compound library, which shows high synthetic efficiency and atom-economic advantages.[11] The commonly devised strategy for tandem reactions involves two or more separated functional groups in the participants, of which one functionality is initiated in the first process and then the others are sequentially subjected to the next process.[12] Recently, three-component tandem reactions of 2-aminopyridine, aldehydes and alkynes have been developed with copper as catalyst for the preparation of imidazo[1,2-*a*]pyridines.[13] This prompted us to design a new tandem reaction route to multi-substituted pyrimidines through the amination-cyclization-oxidation process from amidines, aryl alkynes and aldehydes in a one-pot manner.

Table 1. Selected optimization studies[a]



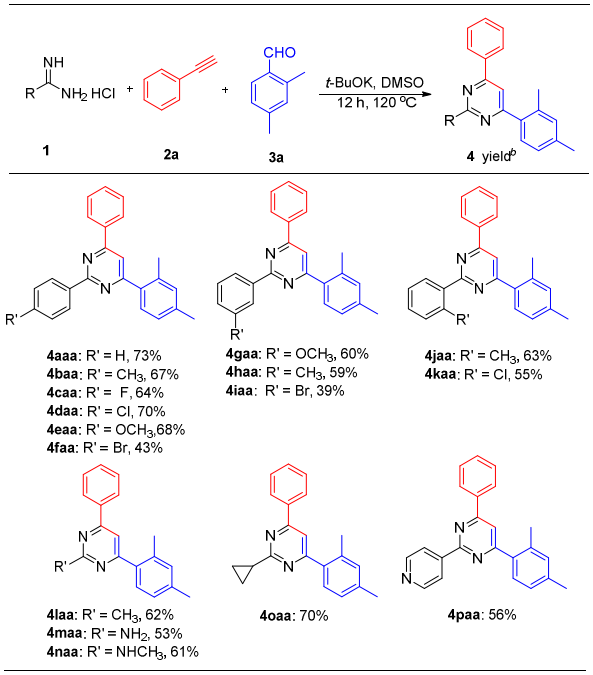
Entry	Base	Solvent	T (°C)	Yield (%)[b]
1	DBU	DMSO	120	36
2	DABCO	DMSO	120	26
3	Et_3N	DMSO	120	24
4	K_3PO_4	DMSO	120	30
5	KOH	DMSO	120	55
6	*t*-BuOK	DMSO	120	62
7	*t*-BuOK	Toluene	120	21
8	*t*-BuOK	CH_3CN	80	47
9	*t*-BuOK	DMF	120	25
10	*t*-BuOK	DMA	120	44
11	*t*-BuOK	1,4-Dioxane	100	31
12	*t*-BuOK	DCE	80	n.d.
13	*t*-BuOK	EtOH	100	n.d.
14	*t*-BuOK	H_2O	120	n.d.
15	-	DMSO	120	trace
16[c]	*t*-BuOK	DMSO	120	73
17[d]	*t*-BuOK	DMSO	120	50
18[e]	*t*-BuOK	DMSO	120	55

[a]Reaction conditions: Unless otherwise noted, all reactions were performed with **1a** (0.20 mmol), **2a** (0.30 mmol), **3a** (0.30 mmol), and base (0.40 mmol) in 1.0 mL solvent under air for 12 h. n.d. = not detected. [b]GC yield based on **1a** with *n*-dodecane as an internal standard. [c]Under N_2. [d]Under O_2. [e]Vacuum protection.

Initially, we began our investigation with easily accessible benzimidamide (**1a**), ethynylbenzene (**2a**) and 2,4-dimethylbenzaldehyde (**3a**) as the model substrates to test the feasibility of our projected transformation process by our previous reports. (Table 1). A preliminary attempt with DBU as base in 1.0 mL DMSO at 120 °C led to 4-(2,4-dimethylphenyl)-2,6-diphenylpyrimidine (**4aaa**) in 36% yield (Table 1, entry 1). Next, using DABCO, Et_3N, and K_3PO_4 as bases, the yields were still not further increased (Table 1, entries 2-4). To our delight, KOH and *t*-BuOK exhibited superior reactivities affording the yields of 55% and 62%, respectively (Table 1, entries 5-6). Different solvents such as toluene, CH_3CN, DMF, DMA, and 1,4-dioxane have been explored, however, they did not enhance the yield of the target product, and DCE, EtOH and H_2O were completely ineffective (Table 1, entries 7-14). Whereas the absence of *t*-BuOK inhibited the reaction performance (Table 1, entry 15).

Encouragingly, when the reaction was performed under N_2 atmosphere, **4aaa** was afforded in 73% yield (Table 1, entry 16). However, the lower yield of **4aaa** was obtained under O_2 atmosphere or vacuum (Table 1, entries 17 and 18). As a consequence, the optimized reaction conditions were comfirmed by using *t*-BuOK (0.40 mmol) in DMSO at 120 ^oC under N_2 (1 atm) for 12 h.

Table 2. Substrate scope of amidines[a]

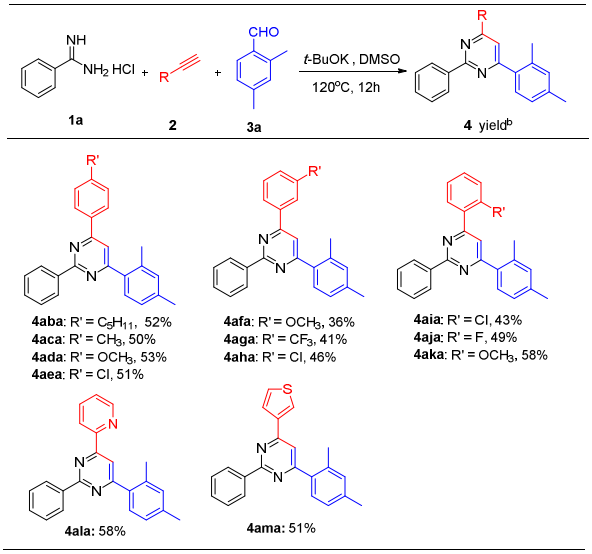


[a]Reaction conditions: Unless otherwise noted, all reactions were performed with **1** (0.2 mmol), **2a** (0.30 mmol), **3a** (0.30 mmol), *t*-BuOK (0.40 mmol) in 1.0 mL solvent under N_2 at 120 ^oC for 12 h. [b]Yields of isolated products.

Next, the scope and generality of this process were investigated under the optimized conditions. We firstly investigated the scope of different substituted amidines with ethynylbenzene (**2a**) and 2, 4-dimethylbenzaldehyde (**3a**) as partners. The results are summarized in Table 2. Generally, arylamidines bearing either electron-donating or electron-withdrawing groups are efficient substrates, providing the desired products **4aaa**–**4kaa** in moderate yields. *ortho*-Substituted arylamidines gave slightly lower yields because of the steric effects. It is worth noting that halogen

groups (Cl, Br) were tolerated, providing the possibility for further functionalization (**4daa**, **4faa**, **4iaa**, **4kaa**). Non-aromatic amidines were also tolerated well, delivering the desired products **4laa**–**4oaa** in moderate yields. Gratifyingly, isonicotinamidine could also be transformed in combination with **2a** and **3a** into the desired products (**4paa**) in moderate yields upon isolation.

Table 3. Substrate scope of aryl alkynes[a]

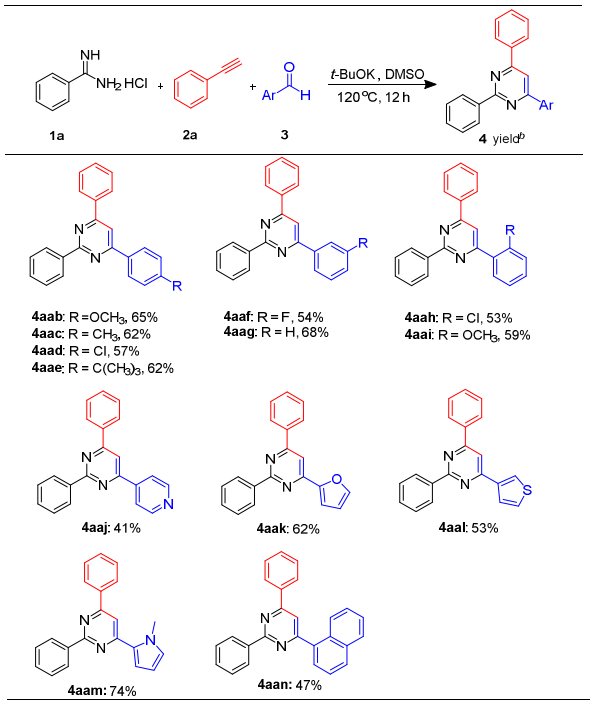


[a]Reaction conditions: Unless otherwise noted, all reactions were performed with **1a** (0.2 mmol), **2** (0.30 mmol), **3a** (0.30 mmol), *t*-BuOK (0.40 mmol) in 1.0 mL solvent under N_2 at 120 °C for 12 h. [b]Yields of isolated products.

After having exhibited a broad scope for substituted amidines, a series of structurally diverse aryl alkynes **2** were next investigated to react with **1a** and **3a** under the same optimized conditions. As shown in Table 3, alkyne derivatives bearing different substitution patterns including F, Cl, CF_3, C_5H_{11}, CH_3 and OCH_3 were found to be well tolerated and smoothly gave the desired products in moderate yields (**4aba**–**4aka**). The experimental results also showed that strong electron-donating groups on the aromatic ring seemed to promote the reaction reactivity slightly, and halide substituents unfavored the formation of products **4**. Moreover, *para*- andmeta-substituted aryl alkynes gave higher yields than those of ortho-substituted substrates.

In addition, 2-ethynylpyridine and 3-ethynylthiophene were found to be compatible and converted to the corresponding products **4ala** and **4ama**. Nonetheless, when the alkyne was used as the substrates, only a trace amount of the corresponding products could be detected.

Table 4. Substrate scope of aryl aldehydes[a]

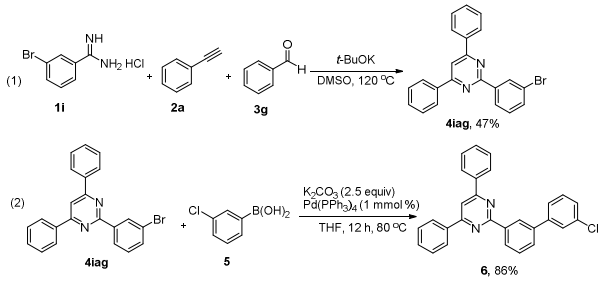


[a]Reaction conditions: Unless otherwise noted, all reactions were performed with **1a** (0.2 mmol), **2a** (0.30 mmol), **3** (0.30 mmol), *t*-BuOK (0.40 mmol) in 1.0 mL solvent under N_2 at 120 °C for 12 h. [b]Yields of isolated products.

Furthermore, we examined the scope of aryl aldehydes using **1a** and **2a** as coupling partners. As shown in Table 4， Benzaldehydes bearing electron-donating or electron-withdrawing groups produced the desired products with moderate yields (**4aab**–**4aai**). Substituents such as -CH_3, -OCH_3, -$C(CH_3)_3$ and other functionalities (F, Cl) on the aryl ring of **3** were well tolerated, and the electronic property of which affected the product yields to some extent. Specifically, electron-rich ones afforded better results than those of electron-deficient ones. Notably, heteroaryl aldehydes were also used as

effective coupling partner to afford the corresponding products in fair yields (**4aaj**, **4aak, 4aal**). Satisfactorily, 1-methyl-1*H*-pyrrole also transformed effectively into our desired product **4aam** in 74% yeild. Much to our delight, substrate with naphthalene was successfully subjected to this reaction system providing **4aan**. However, alkylaldehyde only generated a trace of products.

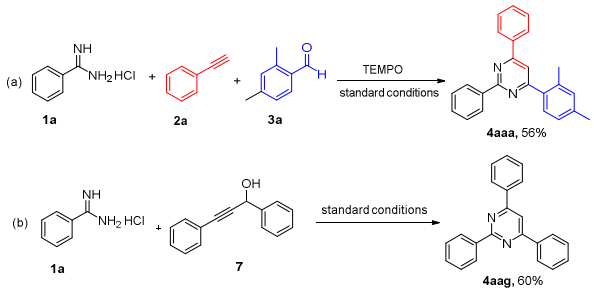
Scheme 1. Application of the pyrimidines products



The pyrimidine of our developed protocol can smoothly proceed the further transformation, which is illustrated in Scheme 1. The Suzuki coupling reaction between **4iag** and **5** successfully provided the corresponding product **6** in good yield. In addition, the product 6 could further transfer to some compounds for an organic optoelectric device, indicating that pyrimidines have potential applications in light emitting devices.[14]

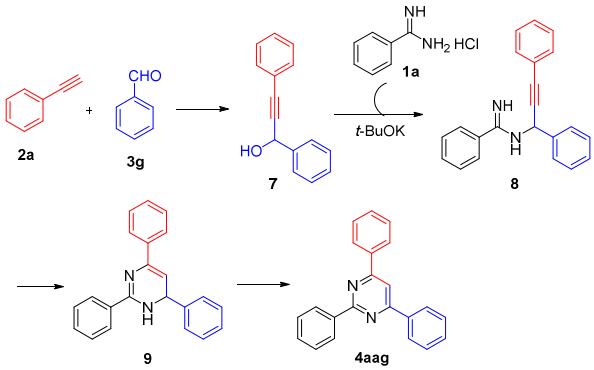
In order to gain more insight into the reaciton mechanism, control experiments were further conducted. In the presence of TEMPO under the standard reaction conditions, **4aaa** was also obtained. These results suggested that a radical pathway should not be involved (Scheme 2, a). Furthermore, when **1a** was reacted with propargylic alcohol **7** under the same conditions, the desired product **4aag** was obtained in 60% yield, indicating that **7** might be a reasonable intermediate for this chemical process (Scheme 2, b).

Scheme 2. Mechanistic studies



Based on the above experimental results in the current study and previous reports,[13, 15]a non-radical pathway mechanism was proposed (Scheme 3). Firstly, ethynylbenzene **2a** reacts with aldehyde **3g** to deliver propargylic alcohol **7**. Intermediate **7** reacts with benzimidamide (**1a**) to generate intermediate **8**, and then further affords the intermediate **9** through intramolecule addition process. Finally, as a result of the oxidability of DMSO ,the oxidation of **9** gives the product **4aag**.[16]

Scheme 3. Possible reaction mechanism



In conclusion, this protocol realizes a base mediated three-component tandem reaction for the synthesis of multi-substituted pyrimidines from amidines, aryl alkynes and aldehydes in one-pot. This novel transformation provides a practical approach for the synthesis of a variety of pyrimidines, showing step-economy, wide substrate scope, good functional group tolerance and mild reaction conditions, which exhibits potential applications in the pharmaceutical industry and material field.

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 (Bruker Avance DRX-400 MHz). IR spectra were obtained with an infrared spectrometer on either potassium bromide pellets or liquid films between two potassium bromide pellets (Bruker Tensor 27). GC−MS (Thermo Trace 1300 GC−Thermo ISO LT) data were obtained using electron ionization. HRMS (MAT 95XP, Thermo) was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). 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 the Synthesis of Pyrimidine Derivatives. A mixture of amidines (0.20 mmol), ethynylbenzene (0.30 mmol) and aldehyde (0.30 mmol), *t*-BuOK (0.40 mmol, 2.0 equiv) was stirred in DMSO (1.0 mL) at 120 ^{o}C under an N_2 (1 atm) atmosphere for 12 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).

4-(2,4-Dimethylphenyl)-2,6-diphenylpyrimidine (4aaa). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Pale yellow solid: 73% yield (49 mg); mp 73−75 °C; IR (KBr, cm^{-1}): ν 2922, 1630, 1520, 1384, 1120, 772; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.75 (d, J = 8.0 Hz, 2H), 8.32 (d, J = 8.0 Hz,2H), 7.77 (s, 1H), 7.62-7.55 (m, 7H), 7.22 (d, J = 8.0 Hz, 2H), 2.62 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100

MHz, $CDCl_3$, ppm): δ 168.2, 164.1, 164.0, 139.5, 138.3, 137.5, 136.5, 135.9, 132.2, 130.8, 130.7, 129.8, 129.0, 128.6, 128.5, 127.3, 127.0, 114.32, 21.3, 20.9; MS (EI, 70 eV) *m/z* 336.35, 259.28, 232.24, 104.14, 77.12; HRMS (ESI) calcd $C_{24}H_{20}N_2Na$ [M + Na]+ m/z 359.1519, found m/z 359.1523.

4-(2,4-Dimethylphenyl)-6-phenyl-2-(p-tolyl)pyrimidine (4baa). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Yellow oil: 67 % yield (47 mg); IR (KBr, cm^{-1}): ν 2920, 1568, 1520, 1453, 1368, 1097, 767; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.56 (d, *J* = 8.0 Hz, 2H), 8.28-8.25 (m, 2H), 7.70 (s, 1H), 7.56-7.51 (m, 4H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* =12.0 Hz, 2H), 2.56 (s, 3H), 2.45 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.1, 164.1, 164.0, 140.8, 139.4, 137.6, 136.5, 135.9, 135.5, 132.1, 130.7, 129.7, 129.2, 128.9, 128.5, 127.3, 126.9, 114.0, 21.6, 21.3, 20.8; MS (EI, 70 eV) *m/z* 350.38, 273.29, 232.26, 154.16, 77.13; HRMS (ESI) calcd $C_{25}H_{23}N_2$ $[M + H]^+$ *m/z* 351.1856, found *m/z* 351.1860.

4-(2,4-Dimethylphenyl)-2-(4-fluorophenyl)-6-phenylpyrimidine (4caa). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. White solid: 64% yield (45 mg); mp 95-97 °C; IR (KBr, cm^{-1}): ν 2920, 1458, 1383, 1028, 953, 756; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.69-8.66 (m, 2H), 8.27-8.24 (m, 2H), 7.72 (s, 1H), 7.57-7.50 (m, 4H), 7.19 (t, *J* = 8.0 Hz, 4H), 2.56 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.2, 164.1, 163.5, 163.1, 139.6, 137.4, 136.4, 135.7, 134.4 (d, *J* = 3.0 Hz), 132.1, 130.8, 130.6 (d, *J* = 8.0 Hz), 129.7, 129.0, 127.3, 126.9, 115.4 (d, *J* = 22.0 Hz), 114.2, 21.3, 20.7; MS (EI, 70 eV) *m/z* 354.38, 277.28, 232.26, 102.15, 77.12; HRMS (ESI) calcd $C_{24}H_{19}FN_2Na[M + Na]^+$ *m/z* 377.1424, found *m/z* 377.1422.

2-(4-Chlorophenyl)-4-(2,4-dimethylphenyl)-6-phenylpyrimidine(4daa). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. White solid: 70% yield (52 mg); mp 123-125 °C; IR (KBr, cm^{-1}): ν 2920, 1571, 1522, 1359, 1088, 762; ^1H NMR

(400 MHz, $CDCl_3$, ppm): δ 8.61 (d, *J* = 8.0 Hz, 2H), 8.26-8.23 (m, 2H), 7.73 (s, 1H), 7.56-7.47 (m, 6H), 7.18 (d, *J* = 12.0 Hz, 2H), 2.55 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.3, 164.2, 163.1, 139.6, 137.3, 136.8, 136.7, 136.4, 135.6, 132.2, 130.9, 129.8, 129.7, 129.0, 128.7, 127.3, 126.9, 114.5, 21.2, 20.7; MS (EI, 70 eV) *m/z* 370.34, 293.26, 232.26, 185.21, 77.13; HRMS (ESI) calcd $C_{24}H_{20}ClN_2$ $[M + H]^+$ *m/z* 371.1310, found *m/z* 371.1311.

4-(2,4-Dimethylphenyl)-2-(4-methoxyphenyl)-6-phenylpyrimidine (4eaa). Using a mixture of petroleum ether-ethyl acetate (30:1) as eluent. Yellow oil : 68% yield (50 mg); IR (KBr, cm^{-1}): ν 2925, 1571, 1519, 1363, 1250, 1173, 1032, 770; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.65 (d, *J* = 8.0 Hz, 2H), 8.28-8.26 (m, 2H), 7.67 (s, 1H), 7.58-7.52 (m, 4H), 7.19 (d, *J* = 12.0 Hz, 2H), 7.05 (d, *J* =12.0 Hz, 2H), 3.90 (s, 3H), 2.57 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.1, 164.0, 163.8, 161.8, 139.4, 137.7, 136.4, 136.0, 132.1, 131.0, 130.7, 130.1, 129.7, 128.9, 127.3, 126.9, 113.8, 113.6, 55.4, 21.3, 20.7; MS (EI, 70 eV) *m/z* 366.41, 289.32, 232.28, 183.31, 77.13; HRMS (ESI) calcd $C_{25}H_{23}N_2O$ $[M +H]^+$ *m/z* 367.1805, found *m/z* 367.1805.

2-(4-Bromophenyl)-4-(2,4-dimethylphenyl)-6-phenylpyrimidine(4faa). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. White solid: 43% yield (36 mg); mp 148-150 °C; IR (KBr, cm^{-1}): ν 3059, 2923, 1577, 1523, 1362, 1014, 769, 691; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.57-8.54 (m, 2H), 8.27-8.24 (m, 2H), 7.74 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.58-7.55 (m, 3H), 7.52 (d, *J* = 4.0 Hz, 1H), 7.19 (d, *J* = 12.0 Hz, 2H), 2.56 (s, 3H), 2.43 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.3, 164.2, 163.2, 139.6, 137.3, 137.2, 136.4, 135.7, 132.2, 131.6, 130.9, 130.1, 129.7, 129.0, 127.3, 127.0, 125.3, 114.5, 21.3, 20.8; MS (EI, 70 eV) *m/z* 415.29, 339.20, 232.26, 154.18, 77.13; HRMS (ESI) calcd $C_{24}H_{19}BrN_2Na$ $[M + Na]^+$ *m/z* 437.0624, found *m/z* 437.0624.

4-(2,4-Dimethylphenyl)-2-(3-methoxyphenyl)-6-phenylpyrimidine (4gaa). Using a mixture of petroleum ether-ethyl acetate (30:1) as eluent. Yellow oil: 60% yield (44 mg); IR (KBr, cm^{-1}): ν 2922, 1425, 1565, 1269, 756, 696; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.29-8.24 (m, 4H), 7.74 (s, 1H), 7.56-7.54 (t, *J* = 10.0 Hz, 4H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 12.0 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 1H), 3.93 (s, 3H), 2.57 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.1, 164.1, 163.8, 159.9, 139.7, 139.5, 137.5, 136.5, 135.8, 132.2, 130.8, 129.8, 129.5, 128.9, 127.3, 126.9, 121.1, 116.7, 114.4, 113.4, 55.4, 21.3, 20.8; MS (EI, 70 eV) *m/z* 366.46, 289.33, 232.28, 183.24, 77.13; HRMS (ESI) calcd $C_{25}H_{23}N_2O[M + H]^+$ *m/z* 367.1805, found *m/z* 367.1807.

4-(2,4-Dimethylphenyl)-6-phenyl-2-(m-tolyl)pyrimidine (4haa). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Yellow oil: 59% yield (41 mg); IR (KBr, cm^{-1}): ν 3043, 2923, 1572, 1361, 766, 694; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.49 (s, 2H), 8.28 (d, *J* = 4.0 Hz, 2H), 7.72 (s, 1H), 7.54 (d, *J* = 12.0 Hz, 4H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 12.0 Hz, 2H), 2.57 (s, 3H), 2.50 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.2, 164.2, 164.1, 139.5, 138.2, 138.0, 137.6, 136.4, 135.9, 132.1, 131.4, 130.7, 129.7, 129.1, 128.9, 128.4, 127.3, 126.9, 125.7, 114.3, 21.6, 21.3, 20.7; MS (EI, 70 eV) *m/z* 350.43, 273.30, 232.27, 154.19, 77.12; HRMS (ESI) calcd $C_{25}H_{22}N_2Na$ $[M + Na]^+$ *m/z* 373.1675, found *m/z* 373.1676.

2-(3-Bromophenyl)-4-(2,4-dimethylphenyl)-6-phenylpyrimidine (4iaa). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. White solid: 39% yield (32 mg); mp 109-111 °C; IR (KBr, cm^{-1}): ν 3063, 2923, 1569, 1356, 764, 695; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.82 (s, 1H), 8.61 (d, *J* = 8.0 Hz, 1H), 8.27-8.25 (m, 2H), 7.75 (s, 1H), 7.64-7.51 (m, 5H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 12.0 Hz, 2H),

2.56 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.3, 164.2, 162.6, 140.3, 139.7, 137.2, 136.4, 135.6, 133.4, 132.2, 131.5, 130.9, 130.0, 129.7, 129.0, 127.3, 127.1, 127.0, 122.8, 114.7, 21.3, 20.7; MS (EI, 70 eV) *m/z* 415.32, 337.23, 232.27, 154.19, 77.13; HRMS (ESI) calcd $C_{24}H_{20}BrN_2$ $[M + H]^+$ *m/z* 415.0804, found *m/z* 415.0808.

4-(2,4-Dimethylphenyl)-6-phenyl-2-(o-tolyl)pyrimidine (4jaa). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Yellow oil : 63% yield (44 mg); IR (KBr, cm^{-1}): ν 3049, 2924, 1572, 1520, 1358, 754, 692; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.26-8.24 (m, 2H), 8.09-8.07 (m, 1H), 7.77 (s, 1H), 7.57-7.52 (m, 4H), 7.41-7.34 (m, 3H), 7.18 (d, *J* = 8.0 Hz, 2H), 2.76 (s, 3H), 2.56 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.0, 167.2, 163.7, 139.4, 138.7, 137.6, 137.4, 136.2, 135.9, 132.0, 131.4, 130.9, 130.8, 129.8, 129.3, 129.0, 127.3, 126.9, 125.9, 113.8, 21.8, 21.3, 20.8; MS (EI, 70 eV) *m/z* 350.40, 273.33, 232.28, 159.97, 77.11; HRMS (ESI) calcd $C_{25}H_{23}N_2$ $[M + H]^+$ *m/z* 351.1856, found *m/z* 351.1862.

2-(2-Chlorophenyl)-4-(2,4-dimethylphenyl)-6-phenylpyrimidine (4kaa). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Yellow oil: 55% yield (41 mg); IR (KBr, cm^{-1}): ν 3059, 2924, 1574, 1520, 1361, 1034, 758; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.25 (t, *J* = 2.0 Hz, 2H), 7.95 (t, *J* = 4.0 Hz, 1H), 7.80 (s, 1H), 7.56-7.51(m, 5H), 7.40 (t, *J* = 4.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 2.56 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.3, 165.1, 164.1, 139.6, 138.3, 137.1, 136.3, 135.6, 133.1, 132.1, 132.0, 130.9, 130.6, 130.2, 129.9, 129.0, 127.5, 126.9, 126.7, 114.6, 21.3, 20.7; MS (EI, 70 eV) *m/z* 370.33, 293.26, 232.25, 154.20, 77.13; HRMS (ESI) calcd $C_{24}H_{19}ClN_2Na$ $[M + Na]^+$ *m/z* 393.1129, found *m/z* 393.1130.

4-(2,4-Dimethylphenyl)-2-methyl-6-phenylpyrimidine (4laa). Using a mixture of petroleum ether-ethyl acetate (30:1) as eluent. Yellow solid: 62% yield (34 mg); mp

84-86 °C; IR (KBr, cm^{-1}): ν 2918, 1641, 1381, 1032, 758, 686; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.11 (t, *J* = 4.0 Hz, 2H), 7.60 (s, 1H), 7.51 (t, *J* = 4.0 Hz, 3H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 4.0 Hz, 2H), 2.87 (s, 3H), 2.44 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.0, 168.0, 164.1, 139.3, 137.4, 135.8, 135.8, 131.9, 130.7, 129.5, 129.0, 127.3, 126.9, 113.9, 26.5, 21.2, 20.3; MS (EI, 70 eV) *m/z* 274.33, 232.24, 197.22, 77.09; HRMS (ESI) calcd $C_{19}H_{19}N_2$ $[M + H]^+$ *m/z* 275.1543, found *m/z* 275.1544.

4-(2,4-Dimethylphenyl)-6-phenylpyrimidin-2-amine (4maa). Using a mixture of petroleum ether-ethyl acetate (10:1) as eluent. Yellow oil: 53% yield (29 mg); IR (KBr, cm^{-1}): ν 3310, 3187, 1620, 1566, 1360, 764, 694; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.02-8.01 (m, 2H), 7.48 (t, *J* = 4.0 Hz, 3H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.13-7.10 (m, 3H), 5.47 (s, 2H), 2.43 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 169.2, 165.5, 163.2, 139.0, 137.7, 136.0, 135.6, 131.8, 130.5, 129.0, 128.8, 127.2, 126.7, 108.0, 21.2, 20.3; MS (EI, 70 eV) *m/z* 275.33, 232.29, 198.25, 77.13; HRMS (ESI) calcd $C_{18}H_{18}N_3$ $[M + H]^+$ *m/z* 276.1495, found *m/z* 276.1495.

4-(2,4-Dimethylphenyl)-N-methyl-6-phenylpyrimidin-2-amine (4naa). Using a mixture of petroleum ether-ethyl acetate (10:1) as eluent. Yellow solid: 61% yield (35 mg); mp 137-139 °C; IR (KBr, cm^{-1}): ν 3268, 2922, 1559, 1350, 759, 688; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.08 (t, *J*=4.0 Hz, 2H), 7.48 (t, *J*=4.0 Hz, 3H), 7.39 (d, *J*=8.0 Hz, 1H), 7.10 (t, *J*=4.0 Hz, 3H), 5.46 (s, 1H), 3.10 (d, *J*=4.0 Hz, 3H), 2.46 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.9, 164.8, 163.1, 138.9, 138.0, 136.4, 135.9, 131.8, 130.3, 129.1, 128.7, 127.1, 126.7, 106.6, 28.4, 21.2, 20.4; MS (EI, 70 eV) *m/z* 289.29, 212.25, 185.22, 77.11; HRMS (ESI) calcd $C_{19}H_{20}N_3$ $[M + H]^+$ *m/z* 290.1652, found *m/z* 290.1659.

2-Cyclopropyl-4-(2,4-dimethylphenyl)-6-phenylpyrimidine (4oaa). Using a mixture of petroleum ether-ethyl acetate (60:1) as eluent. Yellow oil: 70% yield (42 mg); IR (KBr, cm^{-1}): ν 2924, 1574, 1450, 1367, 1034, 930, 768; ^{1}HNMR (400 MHz,$CDCl_3$, ppm): δ 8.13-8.11 (m, 2H), 7.56 (s, 1H), 7.52-7.49 (m, 3H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 2.46 (s, 3H), 2.39 (s, 3H), 1.31-1.28 (m, 2H), 1.12-1.08 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 171.7, 167.7, 163.6, 139.2, 137.5, 136.2, 135.9, 132.0, 130.6, 129.5, 128.9, 127.2, 126.8, 113.4, 21.2, 20.6, 18.5, 10.6; MS (EI, 70 eV) *m/z* 300.34, 285.29, 223.26, 182.21, 77.09; HRMS (ESI) calcd $C_{21}H_{21}N_2$ $[M + H]^+$ *m/z* 301.1699, found *m/z* 301.1705.

4-(2,4-Dimethylphenyl)-6-phenyl-2-(pyridin-4-yl)pyrimidine (4paa). Using a mixture of petroleum ether-ethyl acetate (10:1) as eluent. White solid: 56% yield (38 mg); mp 137-139 °C; IR (KBr, cm^{-1}): ν 3042, 2922, 1730, 1587, 1368, 740, 679; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.81 (d, *J* = 4.0 Hz, 2H), 8.49 (d, *J* = 8.0 Hz, 2H), 8.25 (t, *J* = 4.0 Hz, 2H), 7.80 (s, 1H), 7.56-7.50 (m, 4H), 7.18 (d, *J* = 12.0 Hz, 2H), 2.56 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.5, 164.4, 162.0, 150.4, 145.5, 139.9, 136.9, 136.5, 135.2, 132.3, 131.1, 129.8, 129.1, 127.3, 127.0, 122.3, 115.6, 21.3, 20.8; MS (EI, 70 eV) *m/z* 337.16, 281.03, 260.06, 232.06, 77.03; HRMS (ESI) calcd $C_{23}H_{20}N_3$ $[M + H]^+$ *m/z* 338.1652, found *m/z* 338.1660.

4-(2,4-Dimethylphenyl)-6-(4-pentylphenyl)-2-phenylpyrimidine (4aba). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Yellow oil: 64% yield (52 mg); IR (KBr, cm^{-1}): ν 2925, 1568, 1514, 1356, 753, 690; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.73 (d, *J* = 8.0 Hz, 2H), 8.23 (d, *J* = 8.0 Hz, 2H), 7.73 (s, 1H), 7.55 (d, *J* = 8.0 Hz, 4H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* =12.0 Hz, 2H), 2.74 (t, *J* = 4.0 Hz, 2H), 2.60 (s, 3H), 2.45 (s, 3H), 1.72 (t, *J* = 8.0 Hz, 2H), 1.40 (s, 4H), 0.96 (t, *J* = 4.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.1, 164.1, 164.0, 146.2, 139.4,

138.4, 136.5, 136.0, 135.0, 132.1, 130.5, 129.7, 129.1, 128.5, 128.5, 127.2, 126.9, 114.0, 35.9, 31.5, 31.1, 22.6, 21.3, 20.8, 14.1; MS (EI, 70 eV) *m/z* 406.50, 348.36, 302.37, 259.30, 91.17, 77.13; HRMS (ESI) calcd $C_{29}H_{31}N_2$ $[M + H]^+$ *m/z* 407.2482, found *m/z* 407.2483.

4-(2,4-Dimethylphenyl)-2-phenyl-6-(*p*-tolyl)pyrimidine (4aca). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Yellow oil: 63% yield (44 mg); IR (KBr, cm^{-1}): ν 3031, 2923, 1572, 1517, 1362, 819, 760; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.73 (d, *J* = 4.0 Hz, 2H), 8.21 (d, *J* =8.0 Hz, 2H), 7.72 (s, 1H), 7.56 (t, *J* = 8.0 Hz, 4H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 12.0 Hz, 2H), 2.61 (d, *J* =8.0 Hz, 3H), 2.48 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.1, 164.0, 164.0, 141.1, 139.4, 138.4, 136.5, 136.0, 134.7, 132.1, 130.5, 129.8, 129.7, 128.5, 128.5, 127.2, 126.9, 114.0, 21.5, 21.3, 20.8; MS (EI, 70 eV) *m/z* 350.39, 259.28, 231.25, 77.15; HRMS (ESI) calcd $C_{25}H_{23}N_2$ $[M + H]^+$ *m/z* 351.1856, found *m/z* 351.1864.

4-(2,4-Dimethylphenyl)-6-(4-methoxyphenyl)-2-phenylpyrimidine (4ada). Using a mixture of petroleum ether-ethyl acetate (30:1) as eluent. Pale yellow oil: 67% yield (49 mg); IR (KBr, cm^{-1}): ν 3058, 2926, 1575, 1515, 1364, 826, 761; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.72 (d, *J* = 8.0 Hz, 2H), 8.28 (d, *J* = 8.0 Hz, 2H), 7.68 (s, 1H), 7.55 (m, *J* = 8.0 Hz, 4H), 7.20 (d, *J* =12.0 Hz, 2H), 7.08 (d, *J* =8.0 Hz, 2H), 3.90 (s, 3H), 2.60 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 167.9, 163.9, 163.6, 162.0, 139.4, 138.4, 136.4, 136.0, 132.1, 130.5, 129.9, 129.7, 128.8, 128.5, 128.5, 126.9, 114.3, 113.4, 55.5, 21.3, 20.8; MS (EI, 70 eV) *m/z* 366.35, 259.27, 232.27, 183.12, 77.14; HRMS (ESI) calcd $C_{25}H_{23}N_2O$ $[M + H]^+$ *m/z* 367.1805, found *m/z* 367.1813.

4-(4-Chlorophenyl)-6-(2,4-dimethylphenyl)-2-phenylpyrimidine (4aea). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. White solid: 57% yield (42

mg); mp 116-118 °C; IR (KBr, cm^{-1}): ν 2921, 1571, 1359, 756, 694; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.67-8.64 (m, 2H), 8.22 (d, *J* = 8.0 Hz, 2H), 7.69 (s, 1H), 7.53-7.50 (m, 6H), 7.18 (t, *J* = 8.0 Hz, 2H), 2.57 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.4, 164.1, 162.9, 139.6, 138.1, 137.0, 136.5, 135.9, 135.7, 132.2, 130.7, 129.7, 129.2, 128.5, 128.5, 128.5, 126.9, 114.0, 21.3, 20.8; MS (EI, 70 eV) *m/z* 370.31, 259.27, 207.18, 154.21, 77.15; HRMS (ESI) calcd $C_{24}H_{20}N_2Cl$ $[M+H]^+$ *m/z* 371.1310, found *m/z* 371.1308.

4-(2,4-Dimethylphenyl)-6-(3-methoxyphenyl)-2-phenylpyrimidine (4afa). Using a mixture of petroleum ether-ethyl acetate (30:1) as eluent. Yellow oil: 61% yield (45 mg); IR (KBr, cm^{-1}): ν 2927, 1570, 1524, 1360, 1041, 763; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.68-8.66 (m, 2H), 7.88 (s, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.72 (s, 1H), 7.54-7.50 (m, 4H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.10-7.07 (m, 1H), 3.95 (s, 3H), 2.57 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.2, 164.0, 163.9, 160.2, 139.5, 139.0, 138.2, 136.4, 135.8, 132.1, 130.6, 129.9, 129.7, 128.5, 128.5, 126.9, 119.6, 116.4, 114.4, 112.7, 55.5, 21.3, 20.7; MS (EI, 70 eV) *m/z* 366.35, 259.28, 232.27, 154.20, 77.13; HRMS (ESI) calcd $C_{25}H_{23}N_2O$ $[M+H]^+$ *m/z* 367.1805, found *m/z* 367.1809.

4-(2,4-Dimethylphenyl)-2-phenyl-6-(4-(trifluoromethyl)phenyl)pyrimidine (4aga). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Yellow oil: 53% yield (44 mg); IR (KBr, cm^{-1}): ν 2924, 1570, 1520, 1323, 1124, 819, 756; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.68-8.65 (m, 2H), 8.37 (d, *J* = 8.0 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.75 (s, 1H), 7.55-7.51 (m, 4H), 7.19 (t, *J* = 4.0 Hz, 2H), 2.58 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.7, 164.2, 162.6, 140.9, 139.8, 137.9, 136.5, 135.5, 132.6, 132.2, 130.8, 129.7, 128.5, 128.5, 127.6, 127.0, 125.9 (q, *J* = 4.0 Hz), 125.4, 114.6, 21.3, 20.8; MS (EI, 70 eV) *m/z* 404.37, 300.27, 259.26,

232.24, 77.13; HRMS (ESI) calcd $C_{25}H_{20}F_3N_2$ $[M + H]^+$ *m/z* 405.1573, found *m/z* 405.1579.

4-(3-Chlorophenyl)-6-(2,4-dimethylphenyl)-2-phenylpyrimidine (4aha). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Black oil: 59% yield (44 mg); IR (KBr, cm^{-1}): ν 2922, 1567, 1356, 760, 697; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.67-8.65 (m, 2H), 8.28 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.69 (s, 1H), 7.54-7.46 (m, 6H), 7.19 (d, *J* = 12.0 Hz, 2H), 2.57 (s, 3H), 2.42 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.5, 164.1, 162.7, 139.7, 139.4, 138.0, 136.5, 135.6, 135.1, 132.2, 130.8, 130.7, 130.2, 129.7, 128.5, 127.4, 126.9, 125.3, 114.3, 21.3, 20.8; MS (EI, 70 eV) *m/z* 370.31, 259.30, 231.24, 154.19, 77.13; HRMS (ESI) calcd $C_{24}H_{20}ClN_2$ $[M + H]^+$ *m/z* 371.1310, found *m/z* 371.1311.

4-(2-Chlorophenyl)-6-(2,4-dimethylphenyl)-2-phenylpyrimidine (4aia). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Yellow oil: 43% yield (32 mg); IR (KBr, cm^{-1}): ν 3065, 2924, 1570, 1359, 1233, 700 ;^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.68-8.66 (m, 2H), 8.29-8.28 (m, 1H), 8.14-8.11 (m, 1H), 7.69 (s, 1H), 7.56-7.48 (m, 7H), 7.19 (t, *J* = 8.0 Hz, 2H), 2.57 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.5, 164.1, 162.7, 139.7, 139.4, 138.0, 136.5, 135.6, 135.1, 132.2, 130.9, 130.8, 130.7, 130.2, 129.7, 128.5, 127.4, 126.9, 125.3, 114.3, 21.3, 20.8; MS (EI, 70 eV) *m/z* 370.31, 259.27, 232.28, 185.22, 154.20, 77.15; HRMS (ESI) calcd $C_{24}H_{19}ClN_2Na$ $[M + Na]^+$ *m/z* 393.1129, found *m/z* 393.1134.

4-(2,4-Dimethylphenyl)-6-(2-fluorophenyl)-2-phenylpyrimidine (4aja). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. White solid: 49% yield (35 mg); mp 108-110 °C; IR (KBr, cm^{-1}): ν 2924, 1571, 1364, 1217, 760, 695; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.67-8.64 (m, 2H), 8.45-8.40 (m, 1H), 7.88 (s, 1H), 7.56-7.47 (m, 5H), 7.39-7.35 (m, 1H), 7.24-7.17 (m, 3H), 2.58 (s, 3H), 2.42 (s, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$, ppm): δ 167.9, 164.0, 160.2, 139.5, 138.2, 136.5, 135.7, 132.1, 132.0 (d, *J* = 9.0 Hz), 131.1 (d, *J* = 3.0Hz), 130.6, 129.9, 128.5, 128.4, 126.9, 124.7 (d, *J* = 4.0 Hz), 118.6, 118.5, 116.5 (d, *J* = 23.0 Hz), 100.0, 21.3, 20.8; MS (EI, 70 eV) *m/z* 354.32, 259.28, 232.25, 154.20, 77.14; HRMS (ESI) calcd $C_{24}H_{19}FN_2Na$ $[M + Na]^+$ *m/z* 377.1424, found *m/z* 377.1427.

4-(2,4-Dimethylphenyl)-6-(2-methoxyphenyl)-2-phenylpyrimidine (4aka). Using a mixture of petroleum ether-ethyl acetate (30:1) as eluent. Pale yellow solid: 57% yield (42 mg); mp 130-132 °C; IR (KBr, cm^{-1}): ν 2929, 1568, 1362, 1246, 755, 697; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.75 (t, *J* = 4.0 Hz, 2H), 8.38-8.36 (m, 1H), 8.09 (s, 1H), 7.65-7.50 (m, 5H), 7.28-7.23 (m, 3H), 7.09 (d, *J* = 8.0 Hz, 1H), 3.96 (s, 3H), 2.67 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 166.8, 163.8, 162.6, 158.2, 139.3, 138.6, 136.5, 136.3, 132.1, 131.6, 131.5, 130.4, 130.0, 128.5, 128.4, 127.0, 126.9, 121.2, 119.5, 111.6, 55.7, 21.3, 20.8; MS (EI, 70 eV) *m/z* 366.38, 259.27, 154.20, 77.12; HRMS (ESI) calcd $C_{25}H_{23}N_2O$ $[M + H]^+$ *m/z* 367.1805, found *m/z* 367.1811.

4-(2,4-dimethylphenyl)-2-phenyl-6-(pyridin-2-yl)pyrimidine (4ala). Using a mixture of petroleum ether-ethyl acetate (10:1) as eluent. Green solid: 58% yield (39 mg); mp 118-120 °C; IR (KBr, cm^{-1}): ν 3057, 2923, 1526, 1361, 743, 696; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.79-8.73 (m, 4H), 8.49 (s, 1H), 7.92-7.88 (m, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.60-7.53 (m, 3H), 7.41-7.39 (m, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 2.64 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.8, 163.7, 163.0, 154.8, 149.5, 139.5, 138.2, 137.1, 136.6, 135.7, 132.2, 130.6, 130.0, 128.5, 128.5, 126.9, 125.2, 121.9, 114.7, 21.3, 21.0; MS (EI, 70 eV) *m/z* 337.18, 259.13, 233.16, 78.10; HRMS (ESI) calcd $C_{23}H_{19}N_3Na$ $[M + Na]^+$ *m/z* 360.1471, found *m/z* 360.1478.

4-(2,4-dimethylphenyl)-2-phenyl-6-(thiophen-3-yl)pyrimidine (4ama). Using a mixture of petroleum ether-ethyl acetate (100:1) as eluent. Brown oil: 51% yield (35 mg); IR (KBr, cm^{-1}): ν 2920, 1742, 1569, 1372, 1242, 755, 689; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.71 (d, *J* = 4.0 Hz, 2H), 8.29 (d, *J* = 4.0 Hz, 1H), 7.88 (d, *J* = 4.0 Hz, 1H), 7.58-7.53 (m, 5H), 7.48 (t, *J* = 4.0 Hz, 1H), 7.19 (d, *J* = 12.0 Hz, 2H), 2.62 (d, *J* = 16.0 Hz, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 168.3, 164.1, 159.9, 140.9, 139.5, 138.3, 136.5, 135.8, 132.2, 130.6, 129.7, 128.5, 128.5, 126.9, 126.8, 126.6, 126.2, 114.1, 21.3, 20.8; MS (EI, 70 eV) *m/z* 342.15, 259.10, 223.08, 154.10, 77.06; HRMS (ESI) calcd $C_{22}H_{19}N_2S$ $[M + H]^+$ *m/z* 343.1263, found *m/z* 343.1273.

4-(4-Methoxyphenyl)-2,6-diphenylpyrimidine (4aab). Using a mixture of petroleum ether-ethyl acetate (30:1) as eluent. White solid: 65% yield (44 mg); mp 144-146 °C; IR (KBr, cm^{-1}): ν 3061, 2924, 1571, 1520, 1363, 1247, 754, 691; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.76-8.73 (m, 2H), 8.30-8.26 (m, 4H), 7.93 (s, 1H), 7.58-7.54 (m, 6H), 7.07 (d, *J* = 12.0 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.5, 164.4, 164.2, 162.0, 138.4, 137.7, 130.7, 130.5, 130.0, 128.9, 128.8, 128.5, 128.4, 127.3, 114.3, 109.4, 55.4; MS (EI, 70 eV) *m/z* 338.29, 235.23, 220.21, 132.14, 77.13; HRMS (ESI) calcd $C_{23}H_{19}N_2O$ $[M + H]^+$ *m/z* 339.1492, found *m/z* 339.1494.

2,4-Diphenyl-6-(p-tolyl)pyrimidine (4aac). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Pale silver solid: 62% yield (40 mg); mp 143-145 °C; IR (KBr, cm^{-1}): ν 3045, 2922, 1576, 1521, 1362, 750, 688; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.76 (t, *J* = 4.0 Hz, 2H), 8.30 (t, *J* = 4.0 Hz, 2H), 8.21 (d, *J* = 8.0 Hz, 2H), 7.98 (s, 1H), 7.59-7.54 (m, 6H), 7.37 (d, *J* = 8.0 Hz, 2H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.7, 164.6, 164.5, 141.1, 138.3, 137.7, 134.8, 130.7, 130.6,

129.7, 128.9, 128.5, 128.4, 127.3, 127.2, 109.9, 21.5; MS (EI, 70 eV) *m/z* 322.36, 219.27, 102.18, 77.18; HRMS (ESI) calcd $C_{23}H_{19}N_2$ $[M+H]^+$ *m/z* 323.1543, found *m/z* 323.1549.

4-(4-Chlorophenyl)-2,6-diphenylpyrimidine (4aad). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. White solid: 57% yield (39 mg); mp 161-163 °C; IR (KBr, cm^{-1}): ν 3056, 2922, 1577, 1523, 1361, 752, 688 ;^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.72-8.70 (m, 2H), 8.29-8.23 (m, 4H), 7.96 (s, 1H), 7.57-7.52 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 165.0, 164.6, 163.5, 138.0, 137.4, 137.0, 136.0, 130.9, 130.8, 129.2, 129.0, 128.6, 128.5, 127.3, 110.0; MS (EI, 70 eV) *m/z* 342.29, 239.18, 204.21, 102.15; HRMS (ESI) calcd $C_{22}H_{16}ClN_2$ $[M+H]^+$ *m/z* 343.0997, found *m/z* 343.0998.

4-(4-(*tert*-Butyl)phenyl)-2,6-diphenylpyrimidine (4aae). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Pale yellow solid: 62% yield (45 mg); mp 118-120 °C; IR (KBr, cm^{-1}): ν 3058, 2959, 1574, 1521, 1366, 751, 692; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.77 (d, *J* = 8.0 Hz, 2H), 8.32-8.24 (m, 4H), 8.01 (s, 1H), 7.62-6.56 (m, 8H), 1.42 (d, *J* = 8.0 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.8, 164.6, 164.5, 154.3, 138.3, 137.7, 134.8, 130.7, 130.6, 128.9, 128.5, 128.5, 127.3, 127.1, 125.9, 110.1, 34.9, 31.3; MS (EI, 70 eV) *m/z* 364.40, 349.38, 174.78, 104.16, 77.12; HRMS (ESI) calcd $C_{26}H_{25}N_2[M+H]^+$ *m/z* 365.2012, found *m/z* 365.2019.

4-(3-Fluorophenyl)-2,6-diphenylpyrimidine (4aaf). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. White solid: 54% yield (35 mg); mp 193-195 °C; IR (KBr, cm^{-1}): ν 3060, 2920, 1574, 1529, 1357, 747, 682; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.78-8.72 (m, 2H), 8.32-8.30 (m, 2H), 8.08-8.03 (m, 2H), 7.98 (s, 1H), 7.60-7.52 (m, 7H), 7.29-7.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 165.0,

164.6, 164.3 (d, J = 2.0 Hz), 162.1, 139.9 (d, J = 7.0 Hz), 137.9, 137.3, 130.9 (d, J = 14.0 Hz), 130.4 (d, J = 8.0 Hz), 129.0, 128.9, 128.5, 128.5, 127.3, 122.8 (d, J = 3.0 Hz), 117.6 (d, J = 21.0 Hz), 114.3 (d, J = 21.0 Hz), 110.2; MS (EI, 70 eV) *m/z* 326.26, 223.27, 120.12, 102.13, 77.12; HRMS (ESI) calcd $C_{22}H_{16}FN_2$ $[M + H]^+$ *m/z* 327.1292, found *m/z* 327.1296.

2,4,6-Triphenylpyrimidine (4aag). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. White solid: 68% yield (42 mg); mp 183-185 °C; IR (KBr, cm^{-1}): ν 3053, 2920, 1572, 1525, 1359, 737, 681; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.79-8.78 (m, 2H), 8.33-8.30 (m, 4H), 8.01 (s, 1H), 7.61-7.54 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.8, 164.5, 138.3, 137.6, 130.8, 130.7, 128.9, 128.6, 128.5, 127.3, 110.3; MS (EI, 70 eV) *m/z* 308.34, 205.26, 154.30, 102.13, 76.16; HRMS (ESI) calcd $C_{22}H_{17}N_2$ $[M + H]^+$ *m/z* 309.1386, found *m/z* 309.1389.

4-(2-Chlorophenyl)-2,6-diphenylpyrimidine (4aah). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. White solid: 53% yield (36 mg); mp 124-126 °C; IR (KBr, cm^{-1}): ν 3061, 2924, 1572, 1364, 752, 693; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.74-8.71 (m, 2H), 8.32-8.30 (m, 2H), 8.04 (s, 1H), 7.89-7.87 (m, 2H), 7.60-7.54 (m, 7H), 7.49-7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.7, 164.7, 163.9, 138.0, 137.6, 137.3, 132.5, 131.8, 130.9, 130.8, 130.7, 130.5, 129.0, 128.5, 128.5, 127.4, 127.3, 115.2; MS (EI, 70 eV) *m/z* 342.25, 239.23, 204.26, 136.16, 76.18; HRMS (ESI) calcd $C_{22}H_{15}ClN_2Na$ $[M + Na]^+$ *m/z* 365.0816, found *m/z* 365.0823.

4-(2-Methoxyphenyl)-2,6-diphenylpyrimidine (4aai). Using a mixture of petroleum ether-ethyl acetate (30:1) as eluent. White solid: 59% yield (40 mg); mp 74-76 °C; IR (KBr, cm^{-1}): ν 3061, 2940, 1572, 1365, 1247, 749, 692; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.76-8.74 (m, 2H), 8.33-8.28 (m, 4H), 7.60-7.47 (m, 7H), 7.22-7.18 (m, 1H),

7.08 (d, J = 8.0 MHz, 1H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.3, 163.7, 163.5, 158.2, 138.5, 138.0, 131.6, 131.4, 130.5, 130.4, 128.9, 128.4, 128.4, 127.4, 127.0, 121.2, 115.5, 111.7, 55.8; MS (EI, 70 eV) *m/z* 338.31, 233.26, 206.23, 102.15, 77.16; HRMS (ESI) calcd $C_{23}H_{18}N_2NaO$ $[M + Na]^+$ *m/z* 361.1311, found *m/z* 361.1316.

2,4-Diphenyl-6-(pyridin-4-yl)pyrimidine (4aaj). Using a mixture of petroleum ether-ethyl acetate (10:1) as eluent. Pale yellow solid: 41% yield (25 mg); mp 205-207 °C; IR (KBr, cm^{-1}): ν 3033, 2917, 1568, 1516, 1358, 742, 684 ;^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.85 (d, J = 4.0 Hz, 2H), 8.72-8.70 (m, 2H), 8.30-8.28 (m, 2H), 8.14 (d, J = 8.0 Hz, 2H), 8.03 (s, 1H), 7.58-7.54 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 165.5, 165.0, 162.3, 150.6, 144.9, 137.6, 137.0, 131.2, 131.0, 129.0, 128.6, 128.5, 127.3, 121.2, 110.6; MS (EI, 70 eV) *m/z* 309.31, 206.25, 154.80, 103.13, 77.14; HRMS (ESI) calcd $C_{21}H_{16}N_3$ $[M + H]^+$ *m/z* 310.1339, found *m/z* 310.1343.

4-(Furan-2-yl)-2,6-diphenylpyrimidine (4aak). Using a mixture of petroleum ether-ethyl acetate (50:1) as eluent. Gold solid: 62% yield (37 mg); mp 158-160 °C; IR (KBr, cm^{-1}): ν 3055, 2923, 1551, 1359, 743, 689; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.69-8.67 (m, 2H), 8.31-8.29 (m, 2H), 7.95 (s, 1H), 7.65 (s, 1H), 7.59-7.52 (m, 6H), 7.47 (d, J = 4.0 Hz, 1H), 6.64-6.63 (m, 1H);^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.6, 164.5, 156.4, 152.7, 144.8, 138.0, 137.4, 130.9, 130.7, 128.9, 128.9, 128.4, 127.3, 112.5, 112.1, 108.0; MS (EI, 70 eV) *m/z* 298.30, 195.23, 92.14, 77.15; HRMS (ESI) calcd $C_{20}H_{15}N_2O$ $[M + H]^+$ *m/z* 299.1179, found *m/z* 299.1179.

2,4-diphenyl-6-(thiophen-3-yl)pyrimidine (4aal). Using a mixture of petroleum ether-ethyl acetate (100:1) as eluent. Brown solid: 53% yield (33 mg); mp 166-168 °C; IR (KBr, cm^{-1}): ν 2919, 1637, 1267, 746; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.71 (d, J = 8.0 Hz, 2H), 8.28 (t, J = 4.0 Hz, 3H), 7.89-7.84 (m, 2H), 7.55-7.48 (m,

7H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.7, 164.6, 160.5, 140.9, 138.1, 137.5, 130.8, 130.7, 128.9, 128.5, 128.5, 127.3, 126.7, 126.7, 126.2, 110.1; MS (EI, 70 eV) *m/z* 314.08, 210.07, 184.05, 108.03, 76.08; HRMS (ESI) calcd $C_{20}H_{15}N_2S$ $[M + H]^+$ *m/z* 315.0950, found *m/z* 315.0951.

4-(1-methyl-1H-pyrrol-2-yl)-2,6-diphenylpyrimidine (4aam). Using a mixture of petroleum ether-ethyl acetate (50:1) as eluent. Black solid: 74% yield (46 mg); mp 120-122 °C; IR (KBr, cm^{-1}): ν 2922, 1570, 1526, 1479, 1365, 730, 693; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.69-8.66 (m, 2H), 8.30-8.28 (m, 2H), 7.82 (s, 1H), 7.61-7.56 (m, 6H), 7.02-7.00 (m, 1H), 6.89-6.88 (m, 1H), 6.32-6.31 (m, 1H), 4.27 (d, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 163.8, 163.5, 159.5, 138.6, 137.8, 130.6, 130.5, 130.2, 128.9, 128.9, 128.5, 128.4, 127.2, 113.8, 110.2, 108.5, 38.4; MS (EI, 70 eV) *m/z* 311.25, 207.17, 104.12, 77.09; HRMS (ESI) calcd $C_{21}H_{18}N_3$ $[M + H]^+$ *m/z* 312.1495, found *m/z* 312.1499.

4-(naphthalen-1-yl)-2,6-diphenylpyrimidine (4aan). Using a mixture of petroleum ether-ethyl acetate (100:1) as eluent. Brown solid: 47% yield (34 mg); mp 128-130 °C; IR (KBr, cm^{-1}): ν 3745, 2921, 1565, 1523, 1364, 751, 694; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.75-8.73 (m, 2H), 8.39 (t, *J* = 4.0 Hz, 1H), 8.34-8.32 (m, 2H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.98 (t, *J* = 4.0 Hz, 1H), 7.92 (s, 1H), 7.82 (d, *J* = 4.0 Hz, 1H), 7.66-7.54 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 167.5, 164.5, 164.4, 138.1, 137.3, 136.9, 134.1, 130.9, 130.9, 130.8, 130.2, 129.0, 128.6, 128.6, 128.6, 127.9, 127.4, 127.0, 126.2, 125.5, 125.4, 115.4; MS (EI, 70 eV) *m/z* 358.00, 254.13, 152.09, 104.10, 77.06; HRMS (ESI) calcd $C_{26}H_{19}N_2$ $[M + H]^+$ *m/z* 359.1543, found *m/z* 359.1547.

2-(3-bromophenyl)-4,6-diphenylpyrimidine (4iag). Using a mixture of petroleum ether-ethyl acetate (200:1) as eluent. Yellow soild: 47% yield; mp 142-144 °C; IR

(KBr, cm^{-1}): ν 2922, 1764, 1513, 1255, 1041, 754; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.85 (s, 1H), 8.65 (d, *J* = 8.0 Hz, 1H), 8.27-8.24 (m, 4H), 7.98 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.59-7.53 (m, 6H), 7.40 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.8, 163.1, 140.3, 137.2, 133.5, 131.5, 131.0, 130.0, 129.0, 127.3, 127.1, 122.8, 110.7; MS (EI, 70 eV) *m/z* 386.00, 204.14, 128.23, 102.09, 77.09; HRMS (ESI) calcd $C_{22}H_{16}BrN_2$ $[M + H]^+$ *m/z* 387.0491, found *m/z* 387.0495.

2-(3'-chloro-[1,1'-biphenyl]-3-yl)-4,6-diphenylpyrimidine (6). Using a mixture of petroleum ether-ethyl acetate (100:1) as eluent. White soild: 86% yield; mp 134-136 °C; IR (KBr, cm^{-1}): ν 2922, 1571, 1526, 1264, 756, 693; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.91 (t, *J* = 2.0 Hz, 1H), 8.76-8.74 (m, 1H), 8.30-8.28 (m, 4H), 7.97 (s, 1H), 7.75 (s, 1H), 7.71-7.68 (m, 1H), 7.64-7.57 (m, 8H), 7.46-7.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.8, 164.2, 143.2, 140.0, 138.9, 137.5, 134.7, 130.9, 130.1, 129.4, 129.1, 129.0, 128.2, 127.5, 127.4, 127.4, 127.1, 125.6, 110.5; HRMS (ESI) calcd $C_{28}H_{20}ClN_2$ $[M + H]^+$ *m/z* 419.1310, found *m/z* 419.1315.

1,3-diphenylprop-2-yn-1-ol (7). Using a mixture of petroleum ether-ethyl acetate (5:1) as eluent. Brown oil; IR (KBr, cm^{-1}): ν 3424, 2924, 1596, 1268, 1180, 754, 692; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ 7.71-7.68 (m, 2H), 7.58-7.55 (m, 2H), 7.48-7.35 (m, 6H), 5.75 (s, 1H), 3.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 140.9, 131.9, 128.8, 128.7, 128.5, 128.5, 127.0, 122.7, 89.2, 86.7, 65.1; MS (EI, 70 eV) *m/z* 208.00, 179.11, 152.07, 77.07; HRMS (ESI) calcd $C_{15}H_{12}NaO$ $[M+Na]^+$ *m/z* 231.0780, found *m/z* 231.0776.

ASSOCIATED CONTENT

Supporting Information

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

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

AUTHOR INFORMATION

Corresponding Author

* E-mail: jianghf@scut.edu.cn. Fax: (+86) 20-8711-2906.

* E-mail: cewuwq@scut.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We are grateful to the National Program on Key Research Project (2016YFA0602900), the National Natural Science Foundation of China (21420102003, 21662002, 21602031), Pearl River S&T Nova Program of Guangzhou (201610010160), the Advanced Innovation Research Teams Project of Jiangxi Province (20133BCB24011), and Jiangxi Natural Science Foundation (20151BAB203011 and 20171BAB203010).

REFERENCES

[1] (a) J. H. Ryu, J. A Lee, S. Kim, Y. A. Shin, J. Yang, H. Y. Han, H. J. Son, Y. H. Kim, J. H. Sa, J.-S. Kim, J. Lee, J. Lee, H. Park, *J. Med. Chem.* **2016**, *59*, 10176-10189. (b) F. Varano, D. Catarzi, F. Vincenzi, M. Betti, M. Falsini, A. Ravani, P. A. Borea, V. Colotta, K. Varani, *J. Med. Chem.* **2016**, *59,* 10564-10576. (c) Lagoja, I. M. *Chem. BiodiVersity.* **2005**, *2*, 1-50. (d) G. Joshi, H. Nayyar, S. Kalra, P. Sharma, A. Munshi, S. Singh, R. Kumar, *Chem. Biol. Drug. Des.*, 2017, 1–12. (e) Petrov, V. F. *Mol. Cryst. Liq. Cryst.* **2006**, *457,* 121−149.

[2] (a) W. D. Shipe, S. S. Sharik, J. C. Barrow, G. B. McGaughey, C. R. Theberge, J. M. Uslaner, Y. Yan, J. J. Renger, S. M. Smith, P. J. Coleman, C. D. Cox, *J. Med.*

Chem. **2015**, *58*, 7888-7894. (b) S. Chan, K. Han, R. Qu, L. Tong, Y. Li, Z. Zhang, H. Cheng, X. Lu, A. Patterson, J. Smaill, X. Ren, J. Ding, H. Xie, K. Ding, *Bioorg. Med. Chem. Lett.*, **2015**, *25*, 4277-4281. (c) A. P. Keche, G. D. Hatnapure, R. H. Tale, A. H. Rodge, S. S. Birajdar, V. M. Kamble, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 3445-3448. (d) W. B. Parker, *Chem. Rev*. **2009**, *109*, 2880−2893. (e) N. Azas, P. Rathelot, S. Djekou, F. Delmas, A. Gellis, C. D. Giorgio, P. Vanelle and P. Timon-David, *Farmaco*, **2003**, *58*, 1263–1270. (f) M. Johar, T. Manning, D. Y. Kunimoto and R. Kumar, *Bioorg. Med. Chem.,* **2005**, *13*, 6663–6671. (g) Vilchis-Reyes, M. A.; Zentella, A.; Martínez-Urbina, M. A.; Guzmán, Á.; Vargas, O.; Ramirez Apan, M. T.; Ventura Gallegos, J. L.; Díaz, E. *Eur. J. Med. Chem*. **2010**, *45*, 379-386. (h) A. Agarwal, K. Srivastava, S. K. Puri and P. M. S. Chauhan, *Bioorg. Med. Chem*. **2005**, *13*, 4645–4650. (i) Lee, S.; Lim, D.; Lee, E.; Lee, N.; Lee, H.; Cechetto, J.; Liuzzi, M.; Freitas-Junior, L. H.; Song, J. S.; Bae, M. A.; Oh, S.; Ayong, L.; Park, S. B. *J. Med. Chem*. **2014**, *57*, 7425-7434 .

[3] (a) K. Itami, D. Yamazaki, Jun-ichi Yoshida, *J. Am Chem. Soc*. **2004**, *126*, 15396-15397. (b) K.-T. Wong, T. S. Hung, Y. Lin, C.-C. Wu, G.-H. Lee, S.-M. Peng, C. H. Chou and Y. O. Su, *Org. Lett.*, **2002**, *4*, 513-516. (c) S. Achelle, J. Rodŕguez-López, N. Cabon, F. Robin-le Guen, *RSC Adv.*, **2015**, *5*, 107396–107399.

[4] (a) M. Movassaghi, M. D. Hill, *J. Am. Chem. Soc.* **2006**, *128*, 14254-14255. (b) O. K. Ahmad, M. D. Hill, M. Movassaghi, *J. Org. Chem.* **2009**, *74*, 8460-8463. (c) M. C. Bagley, D. D. Hughes, M. C. Lubinu, E. A. Merritt, P. H. Taylor, N. C. O. Tomkinson, *QSAR Comb. Sci.* **2004**, *23*, 859-867. (d) W. Guo, J. Liao, D. Liu, J. Li, F. Ji, W. Wu and H. Jiang, *Angew.Chem. Int. Ed.* **2017**, *56*, 1289–1293. (e) W. Guo, D. Liu, J. Liao, F. Ji, W. Wu and H. Jiang, *Org. Chem. Front.* **2017**, *4*, 1107–1111.

(f) W. Guo, C. Li, J. Liao, F. Ji, D. Liu, W. Wu and H. Jiang, *J. Org. Chem.* **2016**, *81*, 5538-5546.

[5] H. Kakiya, K. Yagi, H. Shinokubo and K. Oshima, *J. Am. Chem. Soc.*, **2002**, *124*, 9032–9033.

[6] E. Gayon, M. Szymczyk, H. Gérard, E. Vrancken, J.-M. Campagne, *J. Org. Chem.* **2012**, *77*, 9205-9220.

[7] (a) M. C. Bagley, Z. Lin, S. J. A. Pope, *Tetrahedron Lett.* **2009**, *50*, 6818-6823. (b) M. C. Bagley, D. D. Hughes, P. H. Taylor, *Synlett.* **2003**, *2*, 259-261.

[8] (a) N. Deibl, K. Ament, R. Kempe, *J. Am. Chem. Soc.* **2015**, *137*, 12804-12807. (b) N. Deibl, R. Kempe, *Angew. Chem. Int. Ed.* **2017**, *56(6)*, 1663-1666. (c) Müller, T. J. J. Braum, R.; Ansorge, M. *Org. Lett*. **2000**, *2*, 1967-1970. (d)Y. Satoh, K. Yasuda and Y. Obora, Organometallics, **2012**, *31*, 5235–5238. (e) Lin, M.; Chen,Q.; Zhu, Y.; Chen, X.; Cai, J.; Pan, Y.; Zhan, Z. *Synlett* **2011**, *8*,1179-1183.

[9] (a) T. Sasada, F. Kobayashi, N. Sakai, T. Konakahara, *Org. Lett.* **2009**, *11*, 2161-2164. (b) J. Chen, R. Properzi, D. P. Uccello, J. A. Young, R. G. Dushin, J. T. Starr, *Org. Lett.* **2014**, *16*, 4146-4149.

[10] (a) L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115-136. (b) E. Sanchez-Diez, D. L. Vesga, E. Reyes, U. Uria, L. Carrillo, J. L. Vicario, *Org. Lett.* **2016**, *18*, 1270-1273. (c) J.-P. Wan, Y. Jing, C. Hu, S. Sheng, *J. Org. Chem.* **2016**, *81*, 6826-6831.

[11] (a) H.-Y. Lee, H. Y. Kim, H. Tae, B. G. Kim, J. Lee, *Org. Lett.* **2003**, *5*, 3439-3442. (b) J. Shen, X. Wang, X. Lin, Z. Yang, G. Cheng, X. Cui, *Org. Lett.* **2016**, *18*, 1378-1381. (c) T. U. Thikekar, M. Selvaraju, C.-M. Sun, *Org. Lett.* **2016**, *18*, 316-319.

[12] (a) T. G. Minehan, *Acc. Chem. Res.* **2016**, *49*, 1168-1181. (b) J. Ma, Z.-Z Yuan, X.-W, Kong, H. Wang, Y-M. Li, H. Xiao, G. Zhao, *Org. Lett.* **2016**, *18*, 1450-1453.

[13] P. Liu, C.-L. Deng, X. Lei, G.-Q, Lin, *Eur. J. Org. Chem.* **2011**, 7308-7316.

[14] Kim, H.-S.; Yu, E.-S.; Chae, M.-Y.; Lee, H.-J.; Min, S.-H. Heterocyclic organic compounds for organic optoelectronic devices, organic light emitting diodes, and display devices: European Patent NO. 3015527 [P]. 2016-04-05.

[15] (a) S. K. Guchhait, A. L. Chandgude, G. Priyadarshani, *J. Org. Chem.* **2012**, *77*, 4438-4444. (b) M. Lin, Q.-Z. Chen, Y. Zhu, X.-L. Chen, J.-J. Cai, Y.-M. Pan, Z.-P. Zhan, *Synlett*, **2011**, 1179-1183.

[16] (a) G. Hu, J. Xu, P. Li, *Org. Lett.* **2014**, *16*, 6036-6039. (b) J.-F. Zou, W.-S. Huang, L. Li, Z. Xu, Z.-J. Zheng, K.-F. Yang, L.-W. Xu, *RSC Adv.* **2015**, *5*, 30389-30393.