

# One-Pot, Three-Component Synthesis of Novel 4-Phenyl-2-[3-(alkynyl/alkenyl/aryl)phenyl]pyrimidine Libraries via Michael Addition, Cyclization, and C–C Coupling Reactions: A New MCR Strategy

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**Abstract:** Privileged medicinal scaffolds based on the structures of 4-phenyl-2-[3-(alkynyl/alkenyl/aryl)phenyl]-substituted pyrimidines have been synthesized via a single-step, three-component reaction of 3-(dimethylamino)-1-phenylprop-2-en-1-one (enaminone), 3-bromobenzimidamide hydrochloride, and various alkynes/alkenes/arylboronic acids. The mechanism of this multi-component reaction (MCR) involves a Michael addition, cyclization, isomerization, and dehydration, followed by Sonogashira, Heck or Suzuki coupling. This new MCR strategy afforded a new compound library based on pyrimidine framework.

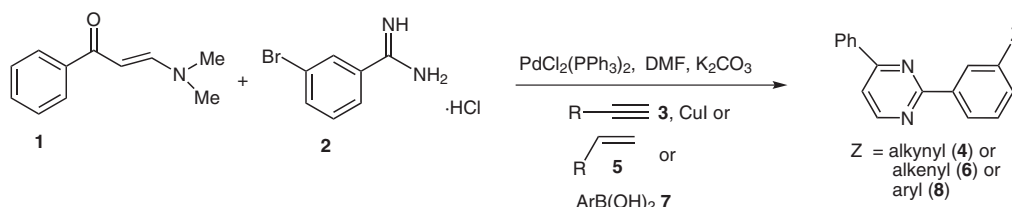
**Key words:** multi-component reactions (MCRs), Michael addition, Pd catalyst, C–C coupling reactions

The synthesis of 'privileged medicinal scaffolds' is highly important as these compounds often act as ligands for a number of functionally and structurally diverse biological receptors and further serve as a platform for developing pharmaceutical agents for diverse applications.<sup>1</sup> For instance, pyrimidine and its derivatives are considered as 'privileged scaffold' due to their potential biological activities such as antihypertensive,<sup>2</sup> antipyretic,<sup>3</sup> antibacterial,<sup>4–6</sup> antifungal,<sup>7,8</sup> anticancer,<sup>9,10</sup> anti-inflammatory,<sup>11,12</sup> and cardio-protective activities.<sup>13</sup> The structural features of pyrimidines are also found in some pesticides,<sup>14</sup> herbicides, and plant growth regulators.<sup>15</sup> Consequently, methodologies for the synthesis of novel pyrimidines or pyrimidine-fused compounds are of particular interest in the medicinal and agrochemical research areas.<sup>16,17</sup>

These vast applications have inspired the development of a number of methods for the preparation of pyrimidine de-

rivatives.<sup>18</sup> In addition to reports about the variation of established protocols, new methods<sup>18</sup> were also described on the union of amine and carbonyl-containing fragments and *N*-vinyl, *N*-aryl amides and nitriles to gather the imperative pyrimidine substructures. Additionally, the advancement of transition metal-catalyzed methodologies for cross-coupling of activated azaheterocycles offer complementary access to substituted azaheterocycles.<sup>19</sup> However, literature studies reveal that, none has been reported on the synthesis of 4-phenyl-2-[3-(alkynyl/alkenyl/aryl)phenyl]-substituted pyrimidine derivatives from enaminone, 3-bromobenzimidamide hydrochloride, and various alkynes/alkenes/arylboronic acids via a single step, one-pot multi-component reaction. Multi-component reactions (MCRs) are powerful strategies for the quick synthesis of diverse and complex organic molecules of potential interest particularly in the area of material science and drug discovery.<sup>20</sup> MCRs have attracted much attention owing to their excellent synthetic efficiency, intrinsic atom economy, high selectivity, procedural simplicity, and environmental friendliness.<sup>20a,21</sup> As a result, the search and discovery of new MCR have attained significant value.<sup>22</sup>

Herein we report a new MCR strategy for the synthesis of 4-phenyl-2-[3-(alkynyl/alkenyl/aryl)phenyl]-substituted pyrimidine derivatives from the reaction of enaminone **1**, 3-bromobenzimidamide hydrochloride (**2**), and various alkynes **3**, alkenes **5** or arylboronic acids **7** in the presence of K<sub>2</sub>CO<sub>3</sub> and Pd catalyst in DMF (Scheme 1).



**Scheme 1** One-pot three-component synthesis of 4-phenyl-2-[3-(alkynyl/alkenyl/aryl)phenyl]-substituted pyrimidines

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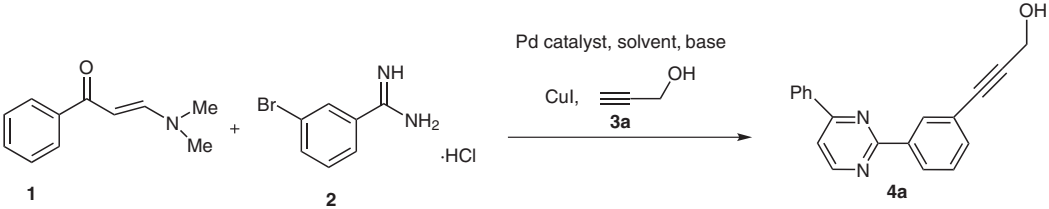
In the present study, our initial objective was to identify well-suited reaction conditions for MCR besides seeking an appropriate Pd catalyst, solvent, and base for the construction of pyrimidine scaffold followed by Sonogashira/Heck/Suzuki coupling in a single step operation. We choose to assess the pyrimidine formation/Sonogashira coupling initially for this purpose. Accordingly, few palladium catalysts, solvents, and bases were examined to determine the effect on the course of MCR of enaminone **1**, 3-bromobenzimidamide hydrochloride (**2**), and prop-2-yn-1-ol (**3a**) in the presence of CuI (Table 1) as a model reaction. Initially, the reaction carried out by using 10% Pd/C catalyst with K<sub>2</sub>CO<sub>3</sub> in DMF at 100 °C for 24 hours afforded the product **4a** in 10% yield (Table 1, entry 1). Later, optimization of the reaction conditions was scrutinized to increase the yield of the product. Towards this direction, a variety of Pd catalysts, solvents, and bases were also examined. The catalysts and solvents, which provided poor to moderate yields, are listed in Table 1 (Table 1, entries 2–10). In contrast, the palladium catalyst, PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, is the only catalyst, which afforded the highest yield (80%) of the desired product **4a** in the pres-

ence of K<sub>2</sub>CO<sub>3</sub> in DMF within 2.5 hours (Table 1, entry 11). When K<sub>2</sub>CO<sub>3</sub> was replaced with an organic base such as Et<sub>3</sub>N, a lower yield (60%) of the product **4a** was noticed within 10 hours in the presence of the same catalyst and solvent (Table 1, entry 12). The same catalyst with K<sub>2</sub>CO<sub>3</sub> in other solvents like DMSO and 1,4-dioxane gave moderate yields of the product **4a** (Table 1, entries 13, 14). The reaction did not proceed in the absence of Pd catalyst (Table 1, entry 15).

With the help of optimized reaction conditions, the further scope and generality of this process for pyrimidine formation and Sonogashira coupling were examined and the results obtained are presented in Table 2.

Encouraged by these results, the possibilities of the construction of pyrimidine scaffold and Heck coupling in a single step were examined. Initially, a reaction was carried out using enaminone **1**, 3-bromobenzimidamide hydrochloride (**2**), and methyl acrylate (**5a**) in the presence of PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> and K<sub>2</sub>CO<sub>3</sub> in DMF at 80–85 °C. The reaction proceeded smoothly to give the corresponding product **6a** in 83% yield. Other alkenes were examined

**Table 1** Optimization of the Reaction Conditions for the Formation of 3-[3-(4-phenylpyrimidin-2-yl)phenyl]prop-2-yn-1-ol<sup>a</sup>



Entry	Catalyst	Solvent	Base	Time (h)	Yield (%) <sup>b</sup>
1	10% Pd/C	DMF	K <sub>2</sub> CO <sub>3</sub>	24	10
2	20% Pd(OH) <sub>2</sub>	DMF	K <sub>2</sub> CO <sub>3</sub>	24	40
3	20% Pd(OH) <sub>2</sub>	DMSO	K <sub>2</sub> CO <sub>3</sub>	24	30
4	20% Pd(OH) <sub>2</sub>	1,4-dioxane	K <sub>2</sub> CO <sub>3</sub>	24	25
5	Pd(dppf)Cl <sub>2</sub>	DMF	K <sub>2</sub> CO <sub>3</sub>	14	55
6	Pd(dppf)Cl <sub>2</sub>	DMSO	K <sub>2</sub> CO <sub>3</sub>	20	40
7	Pd(dppf)Cl <sub>2</sub>	1,4-dioxane	K <sub>2</sub> CO <sub>3</sub>	20	42
8	Pd(PPh <sub>3</sub> ) <sub>4</sub>	DMF	K <sub>2</sub> CO <sub>3</sub>	07	55
9	Pd(PPh <sub>3</sub> ) <sub>4</sub>	DMSO	K <sub>2</sub> CO <sub>3</sub>	10	50
10	Pd(PPh <sub>3</sub> ) <sub>4</sub>	1,4-dioxane	K <sub>2</sub> CO <sub>3</sub>	10	45
<b>11</b>	<b>PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub></b>	<b>DMF</b>	<b>K<sub>2</sub>CO<sub>3</sub></b>	<b>2.5</b>	<b>80</b>
12	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	DMF	Et <sub>3</sub> N	10	60
13	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	DMSO	K <sub>2</sub> CO <sub>3</sub>	07	65
14	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	1,4-dioxane	K <sub>2</sub> CO <sub>3</sub>	07	60
15	–	DMF	K <sub>2</sub> CO <sub>3</sub>	24	0

<sup>a</sup> The reaction was carried out using **1** (0.41 g, 2.339 mmol), **2** (0.5 g, 2.123 mmol), Pd catalyst (0.0712 mmol), base (1.02 g, 7.380 mmol), CuI (0.04 g, 0.21 mmol), and prop-2-yn-1-ol (0.128 g, 2.282 mmol) in a solvent (2.5 mL) at 70–75 °C.

<sup>b</sup> Isolated yield.

**Table 2** Synthesis of 4-Phenyl-2-[3-(alkynyl)phenyl]pyrimidines **4** via Sonogashira Coupling MCR<sup>a</sup>

Entry	Alkyne	Product	Time (h)	Yield (%) <sup>b</sup>	<i>R</i> <sub>f</sub> <sup>c</sup>
1	 <b>3a</b>	 <b>4a</b>	2.5	80	0.3
2	 <b>3b</b>	 <b>4b</b>	3.0	78	0.2
3	 <b>3c</b>	 <b>4c</b>	4.0	70	0.22
4	 <b>3d</b>	 <b>4d</b>	3.4	80	0.4
5	 <b>3e</b>	 <b>4e</b>	3.0	83	0.8
6	 <b>3f</b>	 <b>4f</b>	3.2	85	0.85

<sup>a</sup> All the reactions were carried out using **1** (2.339 mmol), **2** (2.123 mmol), CuI (0.21 mmol), terminal alkyne derivatives **3a–f** (2.282 mmol), DMF (2.5 mL), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (50 mg, 0.0712 mmol), K<sub>2</sub>CO<sub>3</sub> (7.380 mmol) at 70–75 °C.

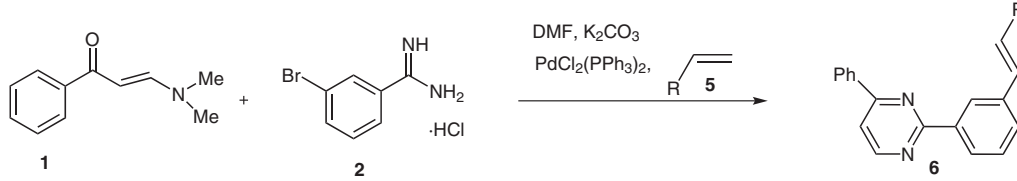
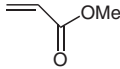
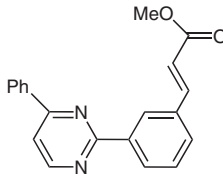
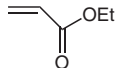
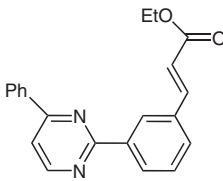
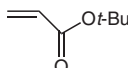
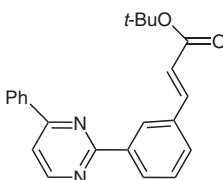

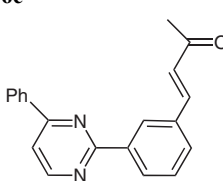

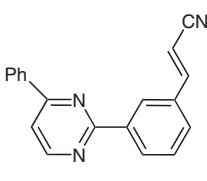
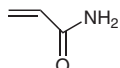
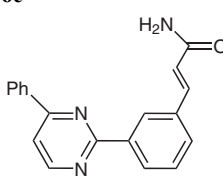
<sup>b</sup> Isolated yield.

<sup>c</sup> Retention factor; eluent: 10% EtOAc in PE.

and the results obtained are presented in Table 3. All reactions required 5–7 hours for completion and to provide the desired alkene derivatives **6a–f**. Based on  $^1\text{H}$  NMR data

all the prepared alkenes were confirmed as *E*-isomers ( $J = 16.8\text{--}16.0\text{ Hz}$ ).

**Table 3** Synthesis of (*E*)-4-Phenyl-2-[3-(alkenyl)phenyl]pyrimidines **6** via Heck Coupling MCR<sup>a</sup>

					
Entry	Alkene	Product	Time (h)	Yield (%) <sup>b</sup>	$R_f^c$
1	 <b>5a</b>	 <b>6a</b>	5.0	83	0.2
2	 <b>5b</b>	 <b>6b</b>	5.4	78	0.25
3	 <b>5c</b>	 <b>6c</b>	6.0	80	0.4
4	 <b>5d</b>	 <b>6d</b>	6.3	78	0.1
5	 <b>5e</b>	 <b>6e</b>	6.0	81	0.1
6	 <b>5f</b>	 <b>6f</b>	7.0	73	0.1

<sup>a</sup> All the reactions were carried out using **1** (2.339 mmol), **2** (2.123 mmol),  $\text{PdCl}_2(\text{PPh}_3)_2$  (50 mg, 0.0712 mmol), alkene derivatives **5a–f** (2.555 mmol),  $\text{K}_2\text{CO}_3$  (7.380 mmol) in DMF (2.5 mL) at 80–85 °C.

<sup>b</sup> Isolated yield.

<sup>c</sup> Retention factor; eluent: 15% EtOAc in PE.

**Table 4** Synthesis of 2-(Biphenyl-3-yl)-4-phenylpyrimidines **8** via Suzuki Coupling MCR<sup>a</sup>

Entry	Arylboronic acid	Product	Time (h)	Yield (%) <sup>b</sup>	<i>R</i> <sub>f</sub> <sup>c</sup>
1	 <b>7a</b>	 <b>8a</b>	2.0	90	0.3
2	 <b>7b</b>	 <b>8b</b>	2.6	85	0.4
3	 <b>7c</b>	 <b>8c</b>	2.3	80	0.4
4	 <b>7d</b>	 <b>8d</b>	3.5	74	0.2
5	 <b>7e</b>	 <b>8e</b>	2.0	85	0.4
6	 <b>7f</b>	 <b>8f</b>	3.2	75	0.45

**Table 4** Synthesis of 2-(Biphenyl-3-yl)-4-phenylpyrimidines **8** via Suzuki Coupling MCR<sup>a</sup> (continued)

Entry	Arylboronic acid	Product	Time (h)	Yield (%) <sup>b</sup>	<i>R</i> <sub>f</sub> <sup>c</sup>
7	 <b>7g</b>	 <b>8g</b>	3.5	78	0.4
8	 <b>7h</b>	 <b>8h</b>	3.3	76	0.5

<sup>a</sup> All the reactions were carried out using **1** (2.339 mmol), **2** (2.123 mmol), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (50 mg, 0.0712 mmol), K<sub>2</sub>CO<sub>3</sub> (7.380 mmol), DMF (2.5 mL), arylboronic acids **7a–h** (2.546 mmol) at 80–85 °C.

<sup>b</sup> Isolated yield.

<sup>c</sup> Retention factor; eluent: 15% EtOAc in PE.

The possibilities for the formation of pyrimidine ring followed by Suzuki coupling in a single step were also examined. Initially, the reaction was carried out using enaminone **1**, 3-bromobenzimidamide hydrochloride (**2**), and 3-cyano-5-fluorophenylboronic acid (**7a**) in the presence of PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> and K<sub>2</sub>CO<sub>3</sub> in DMF at 80–85 °C. The reaction proceeded smoothly and afforded the corresponding product **8a** in 90% yield. Different types of boronic acids were examined and the obtained results are summarized in Table 4. All the reactions were completed within 2–3.5 hours and afforded the desired products **8a–h**.

The plausible mechanism of MCR may proceed via a base-catalyzed Michael addition of 3-bromobenzimidamide hydrochloride (**2**) to the enaminone **1** to form the intermediate **9**. This intermediate sequentially undergoes cyclization, isomerization, and dehydration to give 2-(3-bromophenyl)-4-phenylpyrimidine (**10**), followed by Sonogashira, Heck or Suzuki coupling to afford the 4-phenyl-2-(3-alkynyl/alkenyl/aryl)phenyl-substituted pyrimidines **4**, **6**, and **8** as shown in Scheme 2.

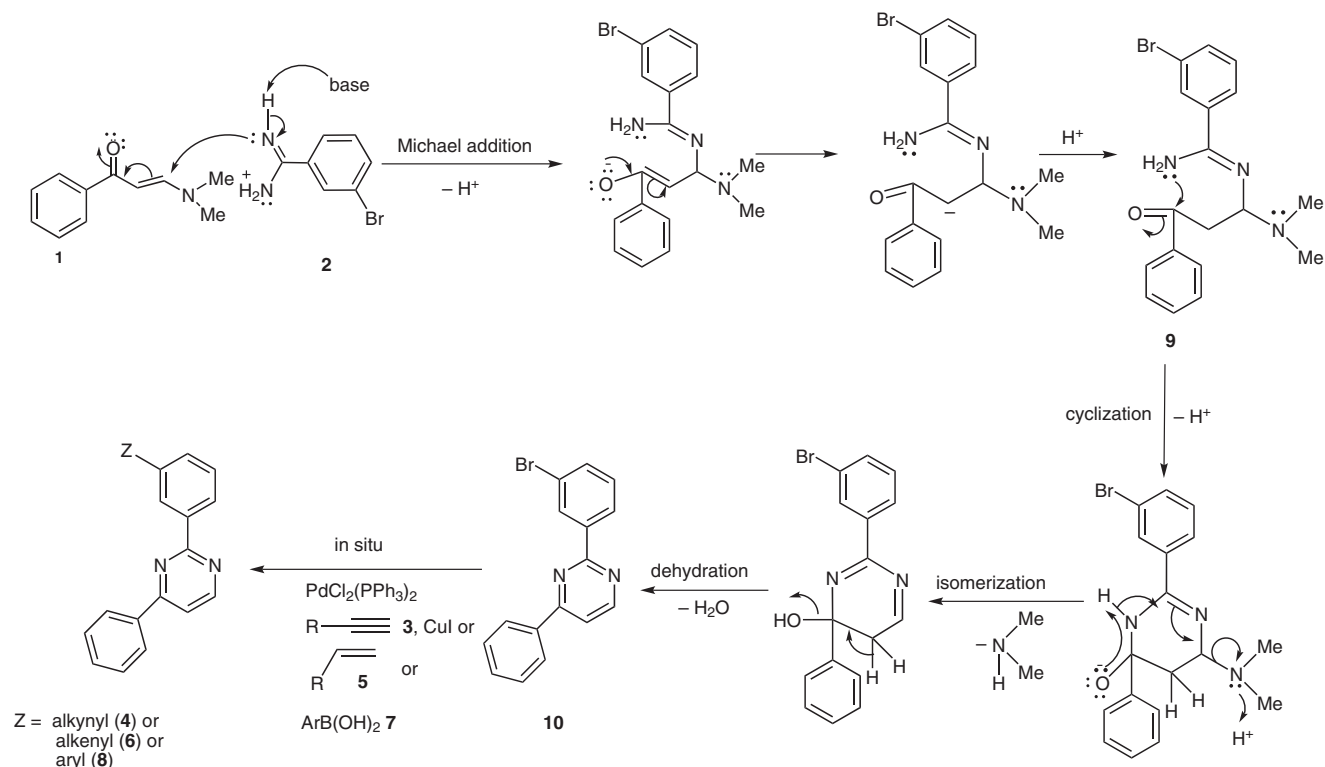
In conclusion, we have developed a new MCR strategy for the synthesis of 4-phenyl-2-[3-(alkynyl/alkenyl/aryl)phenyl]-substituted pyrimidines in high yields from enaminone **1**, 3-bromobenzimidamide hydrochloride (**2**), and various alkynes/alkenes/arylboronic acids via a Michael addition, cyclization, isomerization, dehydration, and followed by Sonogashira/Heck/Suzuki coupling in a single pot. This MCR strategy offers several advantages like

short reaction time, easy isolation of products, simple construction of substituted pyrimidine moiety, and subsequent C–C couplings for the structural elaboration of pyrimidine framework in one pot.

Melting points were determined using a melting point apparatus and are uncorrected. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a Varian 400 MHz spectrometer. Chemical shifts are expressed in parts per million (ppm) and coupling constants in hertz (Hz). Standard abbreviations were used to describe the splitting pattern. High-resolution mass spectra (HRMS) were recorded on a Waters LCT Premier XE mass spectrometer equipped with electrospray ionization (ESI) source. TLC was performed on 0.25 mm Merck silica gel plates and visualized with UV light. Column chromatography was performed on silica gel. Enaminone **1** and 3-bromobenzimidamide hydrochloride (**2**) were prepared according to the known procedure<sup>23,24</sup> and other chemicals and solvents were purchased from Sigma Aldrich and Merck and used directly. Petroleum ether (PE) used refers to the fraction boiling at 60–80 °C.

#### 3-[3-(4-Phenylpyrimidin-2-yl)phenyl]prop-2-yn-1-ol (**4a**); Typical Procedure

In a 25 mL round-bottomed flask were charged enaminone **1** (0.41 g, 2.339 mmol), 3-bromobenzimidamide hydrochloride (**2**; 0.5 g, 2.123 mmol), DMF (2.5 mL), K<sub>2</sub>CO<sub>3</sub> (1.02 g, 7.380 mmol), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (50 mg, 0.0712 mmol), CuI (0.04 g, 0.21 mmol) and prop-1-yn-3-ol (**3a**; 0.128 g, 2.282 mmol) at r.t. Then, the reaction mixture was stirred at 70–75 °C for 2.5 h and the reaction was monitored by TLC (10% EtOAc in PE). After completion of the reaction, the mixture was concentrated under vacuum and the obtained crude product **4a** was purified by column chromatography on silica gel (230–400 mesh) using EtOAc–PE (10% EtOAc–PE); yield: 486 mg (80%); off-white solid; mp 95.1–97.4 °C.



**Scheme 2** Plausible mechanism for the formation of 4-phenyl-2-[3-(alkynyl/alkenyl/aryl)phenyl]-substituted pyrimidines

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.83$  (d,  $J = 4.8$  Hz, 1  $\text{H}_{\text{arom}}$ ), 8.55 (d,  $J = 8.4$  Hz, 2  $\text{H}_{\text{arom}}$ ), 8.21–8.20 (m, 2  $\text{H}_{\text{arom}}$ ), 7.60–7.25 (m, 6  $\text{H}_{\text{arom}}$ ), 4.53 (s, 2 H,  $\text{OCH}_2$ ), 1.97 (br, 1 H, OH).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 163.9$ , 163.7, 157.7, 137.6, 136.6, 131.8 (2 C), 131.0, 128.9 (2 C), 128.1 (2 C), 127.1 (2 C), 124.8, 114.6, 89.1, 85.5, 51.5.

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{19}\text{H}_{15}\text{N}_2\text{O}$ : 287.1184; found: 287.1173.

#### 4-[3-(4-Phenylpyrimidin-2-yl)phenyl]but-3-yn-1-ol (4b)

Purification by column chromatography (15% EtOAc–PE) gave **4b** as an off-white solid; yield: 497 mg (78%); mp 94.2–96.3 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.83$  (d,  $J = 5.6$  Hz, 1  $\text{H}_{\text{arom}}$ ), 8.53 (d,  $J = 8.4$  Hz, 2  $\text{H}_{\text{arom}}$ ), 8.23–8.20 (m, 2  $\text{H}_{\text{arom}}$ ), 7.60 (d,  $J = 5.2$  Hz, 1  $\text{H}_{\text{arom}}$ ), 7.55–7.53 (m, 5  $\text{H}_{\text{arom}}$ ), 3.86 (t,  $J = 6.4$  Hz, 2 H,  $\text{OCH}_2$ ), 2.60 (t,  $J = 6.8$  Hz, 2 H,  $\text{CH}_2$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 163.9$ , 163.8, 157.7, 136.9, 136.8, 131.7 (2 C), 130.9, 128.9 (2 C), 128.0 (2 C), 127.1 (2 C), 126.0, 114.5, 91.4, 81.7, 61.7, 16.0.

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{20}\text{H}_{17}\text{N}_2\text{O}$ : 301.1341; found: 301.1347.

#### 2-Methyl-4-[3-(5-phenylpyrimidin-2-yl)phenyl]but-3-yn-2-ol (4c)

Purification by column chromatography (20% EtOAc–PE) gave **4c** as an off-white solid; yield: 467 mg (70%); mp 95.3–97.7 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.84$  (d,  $J = 5.6$  Hz, 1  $\text{H}_{\text{arom}}$ ), 8.54 (d,  $J = 8.8$  Hz, 2  $\text{H}_{\text{arom}}$ ), 8.23–8.21 (m, 2  $\text{H}_{\text{arom}}$ ), 7.61 (d,  $J = 4.8$  Hz, 1  $\text{H}_{\text{arom}}$ ), 7.62–7.54 (m, 5  $\text{H}_{\text{arom}}$ ), 1.50 [6 H,  $\text{C}(\text{CH}_3)_2$ ].

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 163.9$ , 163.8, 157.8, 137.4, 136.7, 131.8 (2 C), 131.0, 128.9 (2 C), 128.1 (2 C), 127.2 (2 C), 125.0, 114.6, 83.9, 66.3, 31.4, 31.0 (2 C).

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}$ : 315.1497; found: 315.1486.

#### 5-[3-(4-Phenylpyrimidin-2-yl)phenyl]pent-4-yn-1-ol (4d)

Purification by column chromatography (15% EtOAc–PE) gave **4d** as an off-white solid; yield: 533 mg (80%); mp 94.3–96.6 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.83$  (d,  $J = 5.6$  Hz, 1  $\text{H}_{\text{arom}}$ ), 8.52 (d,  $J = 8.4$  Hz, 2  $\text{H}_{\text{arom}}$ ), 8.23–8.20 (m, 2  $\text{H}_{\text{arom}}$ ), 7.60 (d,  $J = 5.2$  Hz, 1  $\text{H}_{\text{arom}}$ ), 7.55–7.52 (m, 5  $\text{H}_{\text{arom}}$ ), 3.85 (t,  $J = 6.4$  Hz, 2 H,  $\text{OCH}_2$ ), 2.61 (t,  $J = 6.8$  Hz, 2 H,  $\text{CH}_2$ ), 1.90 (quint,  $J = 6.4$  Hz, 2 H,  $\text{CH}_2$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 163.8$ , 157.8, 137.7, 136.7, 131.8 (2 C), 131.0, 128.9 (2 C), 128.1 (2 C), 127.2 (2 C), 124.8, 114.6, 85.6, 51.6, 31.9, 14.1.

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}$ : 315.1497; found: 315.1482.

#### 2-[3-(Hex-1-ynyl)phenyl]-4-phenylpyrimidine (4e)

Purification by column chromatography (10% EtOAc–PE) gave **4e** as an off-white solid; yield: 550 mg (83%); mp 109.4–111.5 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.82$  (d,  $J = 5.6$  Hz, 1  $\text{H}_{\text{arom}}$ ), 8.51 (d,  $J = 8.4$  Hz, 2  $\text{H}_{\text{arom}}$ ), 8.23–8.20 (m, 2  $\text{H}_{\text{arom}}$ ), 7.59 (d,  $J = 5.2$  Hz, 1  $\text{H}_{\text{arom}}$ ), 7.55–7.52 (m, 5  $\text{H}_{\text{arom}}$ ), 2.46 (t,  $J = 6.8$  Hz, 2 H,  $\text{CH}_2$ ), 1.64–1.48 (m, 4 H, 2  $\text{CH}_2$ ), 0.98 (t,  $J = 7.2$  Hz, 3 H,  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 162.9$ , 162.8, 156.7, 135.8, 135.7, 130.6 (2 C), 129.9, 127.8 (2 C), 127.0 (2 C), 126.1 (2 C), 125.4, 113.4, 91.5, 79.6, 29.7, 21.0, 18.2, 12.6.

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{22}\text{H}_{21}\text{N}_2$ : 313.1705; found: 313.1693.

#### 2-[3-(Oct-1-ynyl)phenyl]-4-phenylpyrimidine (4f)

Purification by column chromatography (10% EtOAc–PE) gave **4f** as an off-white solid; yield: 614 mg (85%); mp 113.2–115.4 °C.



$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.82 (d,  $J$  = 5.6 Hz, 1  $\text{H}_{\text{arom}}$ ), 8.51 (d,  $J$  = 8.4 Hz, 2  $\text{H}_{\text{arom}}$ ), 8.23–8.20 (m, 2  $\text{H}_{\text{arom}}$ ), 7.59 (d,  $J$  = 5.6 Hz, 1  $\text{H}_{\text{arom}}$ ), 7.54–7.52 (m, 5  $\text{H}_{\text{arom}}$ ), 2.45 (t,  $J$  = 7.2 Hz, 2  $\text{H}$ ,  $\text{CH}_2$ ), 1.67–1.44 (m, 4  $\text{H}$ , 2  $\text{CH}_2$ ), 1.35–1.33 (m, 4  $\text{H}$ , 2  $\text{CH}_2$ ), 0.93 (t,  $J$  = 6.8 Hz, 3  $\text{H}$ ,  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 164.0, 163.8, 157.7, 136.8, 136.7, 131.6 (2 C), 130.9, 128.8 (2 C), 128.0 (2 C), 127.1 (2 C), 126.4, 114.4, 92.6, 80.6, 31.3, 28.67, 28.63, 22.5, 19.5, 14.0

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{24}\text{H}_{25}\text{N}_2$ : 341.2018; found: 341.2025.

#### Methyl (*E*)-3-[3-(4-Phenylpyrimidin-2-yl)phenyl]acrylate (**6a**); Typical Procedure

In a 25 mL round-bottomed flask were charged enaminone **1** (0.41 g, 2.339 mmol), 3-bromobenzimidamide hydrochloride (**2**; 0.5 g, 2.123 mmol), DMF (2.5 mL),  $\text{K}_2\text{CO}_3$  (1.02 g, 7.380 mmol),  $\text{PdCl}_2(\text{PPh}_3)_2$  (50 mg, 0.0712 mmol), and methyl acrylate (**5a**; 0.22 g, 2.555 mmol) at r.t. Then, the mixture was stirred at 80–85 °C for 4–5 h and the reaction was monitored by TLC (10% EtOAc in PE). After completion of the reaction, the mixture was concentrated under vacuum and the obtained crude product **6a** was purified by column chromatography on silica gel (230–400 mesh) using 15% EtOAc–PE; yield: 557 mg (83%); off-white solid; mp 153.2–155.5 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.85 (d,  $J$  = 5.2 Hz, 1  $\text{H}_{\text{arom}}$ ), 8.61 (d,  $J$  = 8.4 Hz, 2  $\text{H}_{\text{arom}}$ ), 8.23–8.21 (m, 2  $\text{H}_{\text{arom}}$ ), 7.79 (d,  $J$  = 16.4 Hz, 1  $\text{H}$ , *trans* H), 7.68–7.54 (m, 6  $\text{H}_{\text{arom}}$ ), 6.56 (d,  $J$  = 16.0 Hz, 1  $\text{H}$ , *trans* H), 3.83 (s,  $\text{OCH}_3$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 167.2, 163.8, 163.6, 157.7, 144.2, 139.4, 136.6, 136.3, 131.0, 128.8 (2 C), 128.6 (2 C), 128.1 (2 C), 127.1 (2 C), 118.5, 114.6, 51.6.

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{20}\text{H}_{17}\text{N}_2\text{O}_2$ : 317.1290; found: 317.1287.

#### Ethyl (*E*)-3-[3-(4-Phenylpyrimidin-2-yl)phenyl]acrylate (**6b**)

Purification by column chromatography (15% EtOAc–PE) gave **6b** as an off-white solid; yield: 546 mg (78%); mp 106.5–108.7 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.84 (d,  $J$  = 5.2 Hz, 1  $\text{H}_{\text{arom}}$ ), 8.60 (d,  $J$  = 8.4 Hz, 2  $\text{H}_{\text{arom}}$ ), 8.23–8.20 (m, 2  $\text{H}_{\text{arom}}$ ), 7.76 (d,  $J$  = 16.4 Hz, 1  $\text{H}$ , *trans* H), 7.67 (d,  $J$  = 8.4 Hz, 2  $\text{H}_{\text{arom}}$ ), 7.62 (d,  $J$  = 4.8 Hz, 1  $\text{H}_{\text{arom}}$ ), 7.56–7.53 (m, 3  $\text{H}_{\text{arom}}$ ), 6.54 (d,  $J$  = 16.0 Hz, 1  $\text{H}$ , *trans* H), 4.29 (q,  $J$  = 6.8 Hz, 2  $\text{H}$ ,  $\text{OCH}_2$ ), 1.36 (t,  $J$  = 6.8 Hz, 3  $\text{H}$ ,  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 166.7, 163.7, 163.6, 157.7, 143.8, 139.3, 136.6, 136.4, 130.9, 128.8 (2 C), 128.6 (2 C), 128.1 (2 C), 127.0 (2 C), 119.0, 114.6, 60.4, 14.2.

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_2$ : 331.1447; found: 331.1455.

#### tert-Butyl (*E*)-3-[3-(4-Phenylpyrimidin-2-yl)phenyl]acrylate (**6c**)

Purification by column chromatography (15% EtOAc–PE) gave **6c** as an off-white solid; yield: 608 mg (80%); mp 94.8–97.1 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.84 (d,  $J$  = 5.2 Hz, 1  $\text{H}_{\text{arom}}$ ), 8.59 (d,  $J$  = 8.8 Hz, 2  $\text{H}_{\text{arom}}$ ), 8.24–8.20 (m, 2  $\text{H}_{\text{arom}}$ ), 7.68–7.53 (m, 7  $\text{H}_{\text{arom}}$  and *trans* H), 6.49 (d,  $J$  = 16.0 Hz, 1  $\text{H}$ , *trans* H), 1.55 (s, 9  $\text{H}$ ,  $t\text{-C}_4\text{H}_9$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 166.1, 163.8, 163.8, 157.8 (2 C), 142.9, 139.1, 136.7, 131.0, 128.9 (2 C), 128.6 (2 C), 128.0 (2 C), 127.1 (2 C), 121.0, 114.6, 80.5, 28.1 (3 C).

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{23}\text{H}_{23}\text{N}_2\text{O}_2$ : 359.1760; found: 359.1761.

#### (*E*)-4-[3-(4-Phenylpyrimidin-2-yl)phenyl]but-3-en-2-one (**6d**)

Purification by column chromatography (10% EtOAc–PE) gave **6d** as an off-white solid; yield: 497 mg (78%); mp 173.1–175.5 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.85 (d,  $J$  = 5.6 Hz, 1  $\text{H}_{\text{arom}}$ ), 8.62 (d,  $J$  = 8.4 Hz, 2  $\text{H}_{\text{arom}}$ ), 8.24–8.21 (m, 2  $\text{H}_{\text{arom}}$ ), 7.70 (d,  $J$  = 8.4 Hz, 1  $\text{H}_{\text{arom}}$ ), 7.63–7.61 (m, 1  $\text{H}_{\text{arom}}$ ), 7.57–7.53 (m, 3  $\text{H}_{\text{arom}}$  and *trans* H), 6.83 (d,  $J$  = 16.0 Hz, 1  $\text{H}$ , *trans* H), 2.42 (s, 3  $\text{H}$ ,  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 198.1, 163.7, 163.5, 157.7, 142.6, 139.6, 136.5, 136.3, 131.0, 128.8 (2 C), 128.6 (2 C), 128.3 (2 C), 127.7, 127.0 (2 C), 114.7, 27.4.

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{20}\text{H}_{17}\text{N}_2\text{O}$ : 301.1341; found: 301.1349.

#### (*E*)-3-[3-(4-Phenylpyrimidin-2-yl)phenyl]acrylonitrile (**6e**)

Purification by column chromatography (20% EtOAc–PE) gave **6e** as an off-white solid; yield: 487 mg (81%); mp 204.1–206.4 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.85 (d,  $J$  = 5.6 Hz, 1  $\text{H}_{\text{arom}}$ ), 8.63 (d,  $J$  = 8.0 Hz, 2  $\text{H}_{\text{arom}}$ ), 8.23–8.21 (m, 2  $\text{H}_{\text{arom}}$ ), 7.64–7.54 (m, 6  $\text{H}_{\text{arom}}$ ), 7.48 (d,  $J$  = 16.4 Hz, 1  $\text{H}$ , *trans* H), 6.00 (d,  $J$  = 16.8 Hz, 1  $\text{H}$ , *trans* H).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 166.5, 162.9, 162.7, 158.6, 138.4, 138.0, 137.2, 136.1, 131.2, 129.0 (2 C), 128.3 (2 C), 127.9 (2 C), 127.1 (2 C), 123.5, 115.1.

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{19}\text{H}_{14}\text{N}_3$ : 284.1188; found: 284.1181.

#### (*E*)-3-[3-(4-Phenylpyrimidin-2-yl)phenyl]acrylamide (**6f**)

Purification by column chromatography (25% EtOAc–PE) gave **6f** as an off-white solid; yield: 467 mg (73%); mp 195.3–197.6 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.98 (d,  $J$  = 5.2 Hz, 1  $\text{H}_{\text{arom}}$ ), 8.57 (d,  $J$  = 8.0 Hz, 2  $\text{H}_{\text{arom}}$ ), 8.37–8.36 (m, 2  $\text{H}_{\text{arom}}$ ), 8.04 (d,  $J$  = 5.6 Hz, 1  $\text{H}_{\text{arom}}$ ), 7.76 (d,  $J$  = 8.4 Hz, 2  $\text{H}_{\text{arom}}$ ), 7.62–7.60 (m, 4  $\text{H}_{\text{arom}}$ ), 7.19 (br, 1  $\text{H}$ , NH), 7.52 (d,  $J$  = 16.4 Hz, 1  $\text{H}$ , *trans* H), 6.76 (d,  $J$  = 16 Hz, 1  $\text{H}$ , *trans* H).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 174.7, 162.9, 162.4, 158.2, 149.4, 147.8, 139.4, 135.9, 135.5, 130.9, 128.7 (2 C), 128.1, 127.7, 126.8 (2 C), 118.1, 115.0, 97.7.

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{19}\text{H}_{16}\text{N}_3\text{O}$ : 302.1293; found: 302.1296.

#### 5-Fluoro-3'-(4-phenylpyrimidin-2-yl)biphenyl-3-carbonitrile (**8a**); Typical Procedure

In a 25 mL round-bottomed flask were charged enaminone **1** (0.41 g, 2.339 mmol), 3-bromobenzimidamide hydrochloride (**2**; 0.5 g, 2.123 mmol), DMF (2.5 mL),  $\text{K}_2\text{CO}_3$  (1.02 g, 7.380 mmol),  $\text{PdCl}_2(\text{PPh}_3)_2$  (50 mg, 0.0712 mmol), and 3-cyano-5-fluorophenylboronic acid (**7a**; 0.42 g, 2.546 mmol) at r.t. The reaction mixture was then stirred at 80–85 °C for 2 h and the reaction was monitored by TLC (15% EtOAc in PE). After completion of the reaction, the mixture was concentrated under vacuum and the obtained crude product **8a** was purified by column chromatography on silica gel (230–400 mesh) using 15% EtOAc–PE; yield: 671 mg (90%); off-white solid; mp 152.5–154.6 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.87 (d,  $J$  = 5.2 Hz, 1  $\text{H}_{\text{arom}}$ ), 8.69 (d,  $J$  = 8.0 Hz, 2  $\text{H}_{\text{arom}}$ ), 8.26–8.23 (m, 2  $\text{H}_{\text{arom}}$ ), 7.76 (s, 1  $\text{H}_{\text{arom}}$ ), 7.70 (d,  $J$  = 8.4 Hz, 2  $\text{H}_{\text{arom}}$ ), 7.66 (d,  $J$  = 5.2 Hz, 2  $\text{H}_{\text{arom}}$ ), 7.63–7.55 (m, 3  $\text{H}_{\text{arom}}$ ), 7.37–7.35 (m, 1  $\text{H}_{\text{arom}}$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 164.1, 163.7 (d,  $J$  = 34.4 Hz, Ar-CF), 161.2, 157.7 (2 C), 144.4, 139.5, 139.5, 138.3, 136.5, 131.1 (2 C), 129.1, 128.9, 127.1 (2 C), 127.1, 126.75, 126.71, 119.0, 118.8, 115.3, 114.8.

HRMS (ESI):  $m/z$  ( $\text{M} + \text{H}$ ) $^+$  calcd for  $\text{C}_{23}\text{H}_{15}\text{FN}_3$ : 352.1250; found: 352.1255.

#### 2-(4'-Methoxybiphenyl-3-yl)-4-phenylpyrimidine (**8b**)

Purification by column chromatography (10% EtOAc–PE) gave **8b** as an off-white solid; yield: 610 mg (85%); mp 159.2–161.5 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.84 (d,  $J$  = 5.6 Hz, 1  $\text{H}_{\text{arom}}$ ), 8.63 (d,  $J$  = 8.4 Hz, 2  $\text{H}_{\text{arom}}$ ), 8.26–8.23 (m, 2  $\text{H}_{\text{arom}}$ ), 7.71 (d,  $J$  = 8.8 Hz,



$^2\text{H}_{\text{arom}}$ ), 7.65–7.62 (m,  $2\text{H}_{\text{arom}}$ ), 7.60 (d,  $J = 5.6\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 7.57–7.54 (m,  $2\text{H}_{\text{arom}}$ ), 7.02 (d,  $J = 8.8\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 3.87 (s, 3 H,  $\text{OCH}_3$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 164.3$ , 163.8, 159.4, 157.7, 142.9, 136.8, 136.0, 132.9, 130.9, 128.8 (2 C), 128.7 (2 C), 128.1 (2 C), 127.1 (2 C), 126.6 (2 C), 116.0, 114.2 (2 C), 55.2.

HRMS (ESI):  $m/z$  ( $M + \text{H}$ ) $^+$  calcd for  $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}$ : 339.1497; found: 339.1506.

#### 2-(3'-Methoxybiphenyl-3-yl)-4-phenylpyrimidine (8c)

Purification by column chromatography (10% EtOAc–PE) gave **8c** as an off-white solid; yield: 574 mg (80%); mp 158.2–160.5 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.85$  (d,  $J = 5.2\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 8.65 (d,  $J = 8.8\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 8.26–8.23 (m,  $2\text{H}_{\text{arom}}$ ), 7.75 (d,  $J = 8.0\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 7.61 (d,  $J = 5.6\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 7.56–7.54 (m,  $3\text{H}_{\text{arom}}$ ), 7.39 (t,  $J = 8.0\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 7.29–7.21 (m,  $3\text{H}_{\text{arom}}$ ), 3.89 (s, 3 H,  $\text{OCH}_3$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 164.2$ , 163.8, 159.9, 157.8 (2 C), 143.1, 142.1, 136.9, 130.9, 129.8, 128.9 (2 C), 128.7 (2 C), 127.2 (2 C), 127.1 (2 C), 119.6, 114.4, 113.0, 112.8, 55.3.

HRMS (ESI):  $m/z$  ( $M + \text{H}$ ) $^+$  calcd for  $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}$ : 339.1497; found: 339.1503.

#### [3'-(4-Phenylpyrimidin-2-yl)biphenyl-3-yl]methanol (8d)

Purification by column chromatography (20% EtOAc–PE) gave **8d** as an off-white solid; yield: 531 mg (74%); mp 123.1–125.7 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.85$  (d,  $J = 5.6\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 8.66 (d,  $J = 8.8\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 8.27–8.24 (m,  $2\text{H}_{\text{arom}}$ ), 7.77 (d,  $J = 8.8\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 7.70 (s,  $1\text{H}_{\text{arom}}$ ), 7.64–7.61 (m,  $2\text{H}_{\text{arom}}$ ), 7.58–7.56 (m,  $3\text{H}_{\text{arom}}$ ), 7.48 (t,  $J = 7.6\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 7.39 (d,  $J = 7.6\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 4.80 (s, 2 H,  $\text{OCH}_2$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 163.9$ , 163.5, 157.3 (2 C), 142.7, 141.1, 140.4, 136.4, 136.3, 130.6 (2 C), 128.6, 128.5, 128.3, 126.8 (2 C), 126.0 (2 C), 125.8, 125.3 (2 C), 114.1, 64.8.

HRMS (ESI):  $m/z$  ( $M + \text{H}$ ) $^+$  calcd for  $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}$ : 339.1497; found: 339.1504.

#### 4-Phenyl-2-[4'-(trifluoromethyl)biphenyl-3-yl]pyrimidine (8e)

Purification by column chromatography (15% EtOAc–PE) gave **8e** as an off-white solid; yield: 679 mg (85%); mp 188.1–190.3 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.88$  (d,  $J = 5.2\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 8.70 (d,  $J = 8.4\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 8.27–8.25 (m,  $2\text{H}_{\text{arom}}$ ), 7.81–7.73 (m,  $6\text{H}_{\text{arom}}$ ), 7.65 (d,  $J = 5.6\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 7.59–7.56 (m,  $3\text{H}_{\text{arom}}$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 164.0$ , 163.9, 157.8 (2 C), 144.1, 141.7, 137.7, 136.8, 131.0 (2 C), 128.9 (2 C), 128.9 (2 C), 127.4 (2 C), 127.3 (2 C), 127.2 (2 C), 125.7, 125.7, 114.6.

HRMS (ESI):  $m/z$  ( $M + \text{H}$ ) $^+$  calcd for  $\text{C}_{23}\text{H}_{16}\text{F}_3\text{N}_2$ : 377.1266; found: 377.1276.

#### 2-(4'-Chlorobiphenyl-3-yl)-4-phenylpyrimidine (8f)

Purification by column chromatography (10% EtOAc–PE) gave **8f** as an off-white solid; yield: 544 mg (75%); mp 150.2–152.5 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.87$  (d,  $J = 5.2\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 8.68 (d,  $J = 8.4\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 8.27–8.25 (m,  $2\text{H}_{\text{arom}}$ ), 7.72 (d,  $J = 8.4\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 7.63–7.56 (m,  $6\text{H}_{\text{arom}}$ ), 7.45 (d,  $J = 8.0\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 164.1$ , 163.8, 157.8 (2 C), 141.9, 138.9, 137.1, 136.8, 133.7, 130.9 (2 C), 128.9, 128.9, 128.8, 128.7 (2 C), 128.3, 127.1 (2 C), 127.0 (2 C), 114.5.

HRMS (ESI):  $m/z$  ( $M + \text{H}$ ) $^+$  calcd for  $\text{C}_{22}\text{H}_{16}\text{ClN}_2$ : 343.1002; found: 343.1015.

#### 2-[3-(2-Methoxypyridin-4-yl)phenyl]-4-phenylpyrimidine (8g)

Purification by column chromatography (25% EtOAc–PE) gave **8g** as an off-white solid; yield: 561 mg (78%); mp 126.4–128.5 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.85$  (d,  $J = 5.6\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 8.66 (d,  $J = 8.4\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 8.49 (d,  $J = 2.4\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 8.25–8.23 (m,  $2\text{H}_{\text{arom}}$ ), 7.89 (d,  $J = 8.8\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 7.68 (d,  $J = 8.4\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ),

7.61 (d,  $J = 5.6\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 7.56–7.54 (m,  $3\text{H}_{\text{arom}}$ ), 6.86 (d,  $J = 8.8\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 4.0 (s, 3 H,  $\text{OCH}_3$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 164.0$ , 163.7, 163.6, 157.7 (2 C), 145.0 (2 C), 139.8, 137.2, 136.7, 130.8, 129.3, 128.8 (2 C), 128.8 (2 C), 127.0 (2 C), 126.4 (2 C), 114.3, 110.7, 53.4.

HRMS (ESI):  $m/z$  ( $M + \text{H}$ ) $^+$  calcd for  $\text{C}_{22}\text{H}_{18}\text{N}_3\text{O}$ : 340.1450; found: 340.1461.

#### 2-(3',4'-Dichlorobiphenyl-3-yl)-4-phenylpyrimidine (8h)

Purification by column chromatography (10% EtOAc–PE) gave **8h** as an off-white solid; yield: 606 mg (76%); mp 121.3–123.7 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.86$  (d,  $J = 5.2\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 8.66 (d,  $J = 8.4\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 8.26–8.23 (m,  $2\text{H}_{\text{arom}}$ ), 7.76 (d,  $J = 2.0\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 7.69 (d,  $J = 8.4\text{ Hz}$ ,  $2\text{H}_{\text{arom}}$ ), 7.64 (d,  $J = 5.2\text{ Hz}$ ,  $1\text{H}_{\text{arom}}$ ), 7.56–7.51 (m,  $5\text{H}_{\text{arom}}$ ).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 164.1$ , 163.9, 157.6 (2 C), 155.3, 140.7, 140.5, 137.4, 136.6, 132.9, 131.7, 131.1, 130.7, 130.7 (2 C), 128.9, 128.9, 128.9, 127.2, 127.0, 126.3 (2 C).

HRMS (ESI):  $m/z$  ( $M + \text{H}$ ) $^+$  calcd for  $\text{C}_{22}\text{H}_{15}\text{Cl}_2\text{N}_2$ : 377.0612; found: 377.0624.

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**Supporting Information** for this article is available online at <http://www.thieme-connect.com/ejournals/toc/synthesis>.

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