Supporting Information

Ruthenium-Catalyzed Direct ortho-Alkynylation of Arenes with Chelation Assistance

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I. General Information.

$^1$H NMR and $^{13}$C NMR spectra were recorded on a JEOL JMN-ECS400 spectrometer in CDCl$_3$ with TMS or CHCl$_3$ as an internal standard. Data are reported as follows: chemical shift in ppm ($\delta$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained on a Horiba FT-700 spectrometer; absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained on a Shimadzu GCMS-QP 2014 and GCMS-QP 5000 instruments with ionization voltages of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303. Column chromatography was performed with SiO$_2$ (Silicycle Siliaflash F60 (230-400 mesh)).

II. Materials.

(Bromoethynyl)triisopropylsilane (2, CAS 111409-79-1) was prepared by AgNO$_3$-catalyzed bromination of (triisopropylsilyl)acetylene with N-bromosuccinimide.\(^1\) [RuCl$_2$(p-cymene)]$_2$ was prepared by following the reported procedure.\(^2\) CsOPiv was prepared from the reaction of PivOH with Cs$_2$CO$_3$.\(^3\) Toluene was dried on a Glass Contour solvent dispensing system (Nikko Hansen & Co., Ltd.). Benzo[h]quinoline (CAS 230-27-3) and 2-phenylpyridine 9 (CAS 1008-89-5) were purchased from Tokyo Kasei Kogyo Co., Ltd.

III. Synthesis of the Starting Materials.

2-(2-Methylphenyl)pyridine 1 (CAS 10273-89-9), 3-methyl-2-phenylpyridine 12 (CAS 10273-90-2), 3-methyl-2-(4-methoxyphenyl)pyridine 14 (CAS 25363-50-2), 3-methyl-2-(4-fluorophenyl)pyridine 22 (CAS 101419-76-5), 2-(1-naphthalenyl)pyridine 26 (CAS 76759-26-7), 2-(2-thienyl)pyridine 28 (CAS 3319-99-1) and 4,6-bis(4-fluorophenyl)pyrimidine (CAS 168915-00-2) 30 were prepared by the nickel-catalyzed cross-coupling reaction of the corresponding 2-arylmagnesium bromides with 2-bromopyridine, 2-bromo-3-methylpyridine or 4,6-dichloropyrimidine.\(^4\) 1-(2-Methylphenyl)-1H-pyrazole (CAS 20157-44-2) was prepared by the Cu-catalyzed N-arylation with iodobenzene.\(^5\) 2-(2-Methylphenyl)pyrimidine (CAS 188527-65-3), 2-(4-(N,N-dimethylamino)phenyl)-3-methylpyridine 16 (CAS 31640-78-5), N-methyl-N-(4-(3-methyl-2-pyridinyl)phenyl)acetamide 18 and 2-(4-acetylphenyl)-3-methylpyridine 20 (CAS 296776-87-9) were prepared by the Pd-catalyzed Suzuki-coupling reaction.\(^6\)

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4,5-Dihydro-2-(2-methylphenyl)oxazole (CAS 43221-62-1) was prepared by the reaction of 2-methylbenzoyl chloride with 2-aminoethanol, followed by dehydration using SOCl₂. 7

2-(2-Methylphenyl)-1H-benzimidazole (CAS 2967-64-6) and 2-(1-naphthalenyl)-1H-benzimidazole (CAS 2562-81-4) 34 were prepared by the reaction of 1,2-phenylenediamine and the corresponding aldehydes in the presence of 1,4-benzoquinone. 8 Spectroscopic data for new compounds are shown below.

2-(4-(V,N-Dimethylamino)phenyl)-3-methylpyridine (16) [CAS: 31640-78-5].

\[
\begin{align*}
&\text{Me}_2\text{N} \\
&\text{C} = \text{N} \\
&\text{CH}_3 \quad \text{CH}_3
\end{align*}
\]

Rf 0.17 (hexane/EtOAc = 3/1). Pale yellow oil. Bp =135 °C (1.5 mmHg). ¹H NMR (CDCl₃, 399.78 MHz) δ 2.41 (s, 3H), 3.01 (s, 6H), 6.78-6.81 (m, 2H), 7.10 (dd, J = 7.6, 4.6 Hz, 1H), 7.46-7.55 (m, 3H), 8.50 (dd, J = 4.6, 1.4 Hz, 1H); ¹³C NMR (CDCl₃, 100.53 MHz) δ 20.51, 40.49, 111.81, 121.03, 128.61, 129.96, 130.41, 138.43, 146.85, 150.14, 158.66; IR (neat) 3045 m, 2887 m, 2802 m, 1612 s, 1581 m, 1523 s, 1421 s, 1356 s, 1227 s, 1196 s, 1169 s, 1117 m, 1065 m, 947 m, 825 s, 791 s; MS m/z (relative intensity, %) 212 (M⁺, 63), 211 (100), 195 (19), 167 (14), 105 (25). HRMS Calcd for C₁₄H₁₆N₂: 212.1312; Found: 212.1312.

N-Methyl-N-(4-(3-methyl-2-pyridinyl)phenyl)acetamide (18).

\[
\begin{align*}
&\text{CH}_3 \\
&\text{C} = \text{N} \\
&\text{O} \\
&\text{C} = \text{H}
\end{align*}
\]

Rf 0.11 (EtOAc). White solid. Mp = 140-141 °C. ¹H NMR (CDCl₃, 399.78 MHz) δ 1.94 (s, 3H), 2.40 (s, 3H), 3.32 (s, 3H), 7.22 (dd, J = 7.8, 5.0 Hz, 1H), 7.28 (d, J = 8.2 Hz, 2H), 7.59-7.63 (m, 3H), 8.54 (d, J = 5.0 Hz, 1H); ¹³C NMR (CDCl₃, 100.53 MHz) δ 19.95, 22.46, 37.09, 122.38, 126.74, 130.31, 130.72, 138.63, 140.02, 144.09, 147.06, 157.35, 170.52; IR (KBr) 3043 w, 2945 w, 1651 s, 1603 m, 1543 m, 1427 m, 1298 w, 854 w, 810 m, 594 m; MS m/z (relative intensity, %) 240 (M⁺, 38), 198 (23), 197 (100), 167 (11), 56 (51). HRMS Calcd for C₁₅H₁₆N₂O: 240.1263; Found: 240.1261.

Methyl 4-(3-methyl-2-pyridinyl)benzoate (20).

Rf 0.11 (hexane/EtOAc = 5/1). White solid. Mp = 61-62 °C. $^1$H NMR (CDCl$_3$, 399.78 MHz) δ 2.36 (s, 3H), 3.95 (s, 3H), 7.23 (dd, $J = 7.8$, 4.6 Hz, 1H), 7.61-7.63 (m, 3H), 8.12-8.15 (m, 2H), 8.55 (dd, $J = 4.7$, 1.4 Hz, 1H); $^{13}$C NMR (CDCl$_3$, 100.53 MHz) δ 19.93, 52.16, 122.58, 129.04, 129.43, 130.92, 138.68 (two overlapping peaks), 145.01, 147.11, 157.44, 166.90; IR (KBr) 3051 w, 2993 w, 2952 w, 1724 s, 1610 w, 1577 m, 1435 m, 1281 s, 1182 m, 1109 s, 1016 m, 866 m, 758 m; MS m/z (relative intensity, %) 227 (M$^+$, 27), 226 (100), 212 (20), 196 (10), 168 (20), 167 (37), 166 (12), 98 (17), 84 (25), 84 (16). HRMS Calcd for C$_{14}$H$_{13}$NO$_2$: 227.0946; Found: 227.0945.

### IV. Optimization Studies.

**Table S1.** Effect of Additives for the Ru-Catalyzed Alkynylation of 1 with 2.$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additive</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CoOPiv (1 equiv)</td>
<td>toluene</td>
<td>62</td>
</tr>
<tr>
<td>2</td>
<td>CoOAc (1 equiv)</td>
<td>toluene</td>
<td>35</td>
</tr>
<tr>
<td>3</td>
<td>Cs$_2$CO$_3$ (1 equiv)</td>
<td>toluene</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>AgOAc (1 equiv)</td>
<td>toluene</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>FluOH (1 equiv.), Cs$_2$CO$_3$ (1 equiv.)</td>
<td>toluene</td>
<td>49</td>
</tr>
<tr>
<td>6</td>
<td>1-AcCO$_2$H (1 equiv.), Cs$_2$CO$_3$ (1 equiv.)</td>
<td>toluene</td>
<td>22</td>
</tr>
<tr>
<td>7</td>
<td>FluOH (1 equiv.), Cs$_2$CO$_3$ (0.5 equiv.)</td>
<td>toluene</td>
<td>54</td>
</tr>
<tr>
<td>8</td>
<td>FluOH (1 equiv.), Li$_2$CO$_3$ (0.5 equiv.)</td>
<td>toluene</td>
<td>11</td>
</tr>
<tr>
<td>9</td>
<td>FluOH (1 equiv.), Na$_2$CO$_3$ (0.5 equiv.)</td>
<td>toluene</td>
<td>27</td>
</tr>
<tr>
<td>10</td>
<td>FluOH (1 equiv.), K$_2$CO$_3$ (0.5 equiv.)</td>
<td>toluene</td>
<td>55</td>
</tr>
<tr>
<td>11</td>
<td>CoOPiv (1 equiv)</td>
<td>dioxane</td>
<td>59</td>
</tr>
<tr>
<td>12</td>
<td>CoOPiv (1 equiv)</td>
<td>DCE</td>
<td>36</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions, unless otherwise specified: 2-(2-methylphenyl)pyridine 1 (0.30 mmol), bromoalkyne 2 (0.36 mmol), [RuCl$_2$(p-cymene)]$_2$ (0.015 mmol), additive, solvent (1 mL), 90 °C, 15 h.
V. General Procedure for Ruthenium-Catalyzed Direct Alkynylation: Ruthenium-Catalyzed Reaction of 1 with 2 (Table 1, entry 9).

To an oven-dried 5 mL screw-capped vial, 2-(2-methylphenyl)pyridine 1 (51 mg, 0.30 mmol), (bromoethyl)trisopropylsilane 2 (120 mg, 0.45 mmol), [RuCl2(p-cymene)]2 (9.0 mg, 0.015 mmol), CsOPiv (110 mg, 0.45 mmol) and toluene (1.0 mL) were added under a gentle stream of nitrogen. The mixture was stirred for 15 h at 100 °C followed by cooling. The mixture was diluted with EtOAc (10 mL) and washed with NaOH aq. (1 M, 2 × 10 mL). The aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO4, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: hexane/EtOAc= 10/1) to afford the desired alkynylated product 3 (77 mg, 74%) as a colorless oil.

VI. Spectroscopic Data for Alkynylated Products (Table 2 and 3, Scheme 1).

For the synthesis of the following compounds, the general procedure shown above was applied to the corresponding N-heteroaryl arenes unless otherwise noted.

2-(2-Methyl-6-((triisopropylsilyl)ethynyl)phenyl)pyridine (3).

\[
\begin{align*}
 &\text{TIPS} \\
 &\text{N} \\
 &\text{aryl} \end{align*}
\]

74% yield. Rf 0.21 (hexane/EtOAc = 10/1). Colorless oil. Bp = 140 °C (1 mmHg). 1H NMR (CDCl3, 399.78 MHz) δ 0.90-0.94 (m, 21H), 2.11 (s, 3H), 7.22-7.26 (m, 3H), 7.37-7.44 (m, 2H), 7.72 (ddd, J = 7.8, 7.7, 1.9 Hz, 2H), 8.67-8.69 (m, 1H); 13C NMR (CDCl3, 100.53 MHz) δ 111.05, 18.48, 20.10, 93.70, 105.78, 121.85, 122.80, 124.97, 127.68, 130.27, 130.34, 135.95, 136.35, 142.92, 149.21, 158.84; IR (neat) 3062 m, 2943 s, 2864 s, 2148 s, 1589 s, 1462 s, 1423 s, 1383 s, 1252 m, 1020 s, 993 s, 883 s, 789 s, 748 s; MS m/z (relative intensity, %) 349 (M+, 1), 308 (13), 307 (48), 306 (100), 264 (15), 220 (21), 125 (29), 117 (20). HRMS Calcd for C23H31NSi: 349.2226; Found: 349.2227.

2-(2-Methyl-6-((triisopropylsilyl)ethynyl)phenyl)pyrimidine (4).
The general procedure was applied to 2-(2-tolyl)pyrimidine except that the reaction was run at 120 °C. 62% yield. Rf 0.29 (hexane/Et₂O = 2/1). Brown oil. ¹H NMR (CDCl₃, 399.78 MHz) δ 0.92-0.94 (m, 21H), 2.13 (s, 3H), 7.22-7.28 (m, 3H), 7.44 (d, J = 6.8 Hz, 1H), 8.86 (d, J = 5.0 Hz, 2H); ¹³C NMR (CDCl₃, 100.53 MHz) δ 11.06, 18.47, 19.61, 93.65, 105.22, 119.10, 122.34, 128.23, 130.25, 130.44, 135.68, 141.62, 157.04, 167.51; IR (neat) 3064 w, 3039 w, 2942 s, 2892 s, 2863 s, 2360 m, 2337 m, 2150 m, 1560 s, 1461 s, 1405 s, 1253 m, 1160 w, 1106 w, 1074 m, 1043 m, 1016 m, 995 m, 943 m, 919 w, 883 s, 817 m, 788 s, 750 m, 728 m, 673 s, 636 m; MS m/z (relative intensity, %) 350 (M⁺, 1), 309 (13), 308 (52), 307 (100), 279 (11), 265 (30), 237 (12), 222 (13), 221 (15), 118 (11). HRMS Calcd for C₂₂H₃₀N₂Si: 350.2178; Found: 350.2175.

1-(2-Methyl-6-((triisopropylsilyl)ethynyl)phenyl)-1H-pyrazole (5).

64% yield. Rf 0.30 (hexane/EtOAc = 1/1). Colorless oil. ¹H NMR (CDCl₃, 399.78 MHz) δ 0.98 (brs, 21H), 2.08 (s, 3H), 6.40 (t, J = 2.1 Hz, 1H), 7.25-7.30 (m, 2H), 7.42-7.44 (m, 1H), 7.59 (d, J = 3.2 Hz, 1H), 7.69 (d, J = 1.3 Hz, 1H); ¹³C NMR (CDCl₃, 100.53 MHz) δ 11.09, 17.55, 18.50, 95.33, 102.25, 105.74, 122.29, 128.49, 130.79, 130.86, 131.18, 136.66, 140.06, 141.27; IR (neat) 3072 w, 2943 s, 2893 s, 2866 s, 2154 s, 1518 s, 1468 s, 1389 s, 750 m, 1082 m, 1016 s, 995 s, 941 s, 883 s; MS m/z (relative intensity, %) 338 (M⁺, 3), 297 (16), 296 (55), 295 (100), 267 (19), 225 (13), 119 (13), 112 (13), 59 (13). HRMS Calcd for C₂₁H₃₀N₂Si: 338.2178; Found: 338.2180.

2-(2-Methyl-6-((triisopropylsilyl)ethynyl)phenyl)-1H-benso[d]imidazole (6).

74% yield. Rf 0.40 (hexane/EtOAc = 2/1). Pale brown solid. Mp = 200-201 °C. ¹H NMR (CDCl₃, 399.78 MHz) δ 0.87 (brs, 21H), 7.18-7.28 (m, 4H), 7.41 (d, J = 7.8 Hz, 1H), 7.52 (brs, 2H); ¹³C NMR (CDCl₃, 100.53 MHz) δ 10.99, 18.32, 20.42, 94.86, 105.09, 122.22 (two overlapping peaks), 123.73, 129.06, 130.50, 130.58, 132.94, 138.78 (two overlapping peaks), 149.99; IR (neat) 3062 m, 2943 s, 2866 s, 2150 m, 1585 w, 1460 s, 1412 s, 1365 m, 1275 m, 1074 m, 910 m, 883 m, 742 s, 677 s; MS m/z (relative intensity, %) 388 (M⁺, 12), 347 (13), 346 (48), 345 (100), 235 (13). HRMS Calcd
2-(2-Methyl-6-((triisopropylsilyl)ethynyl)phenyl)-4,5-dihydrooxazole (7).

The general procedure was applied to 2-(2-tolyl)-4,5-dihydrooxazole except that the reaction was run at 130 °C. The alkynylated product was isolated by GPC.

18% yield. Rf 0.34 (hexane/EtOAc = 2/1). Colorless oil. $^1$H NMR (CDCl$_3$, 399.78 MHz) $\delta$ 1.11 (brs, 21H), 2.33 (s, 3H), 4.08 (t, $J$ = 9.6 Hz, 2H), 4.41 (t, $J$ = 9.6 Hz, 2H), 7.16 (d, $J$ = 7.8, 6.9 Hz, 1H), 7.37 (d, $J$ = 6.9 Hz, 1H); $^{13}$C NMR (CDCl$_3$, 100.53 MHz) $\delta$ 11.24, 18.60, 19.54, 55.37, 67.54, 93.68, 104.64, 123.18, 129.14, 129.94, 130.43, 131.65, 137.22, 163.83; IR (neat) 3064 w, 2943 s, 2866 s, 2152 m, 1668 s, 1464 s, 1252 m, 1047 s, 941 m, 883 m, 679 s; MS m/z (relative intensity, %) 341 (M$^+$, 3), 299 (33), 257 (31), 256 (100), 254 (19), 229 (14), 228 (33), 226 (36), 214 (14), 212 (28), 199 (13), 198 (70), 186 (11), 185 (12), 184 (68), 168 (17), 121 (14), 107 (10), 100 (31), 59 (18). HRMS Calcd for C$_{21}$H$_{31}$NOSi: 341.2175; Found: 341.2168.

10-((Triisopropylsilyl)ethynyl)benzo[h]quinoline (8).

The general procedure was applied to benzo[h]quinoline except that the reaction was run at 130 °C. The alkynylated product was isolated by GPC.

19% yield. Rf 0.37 (hexane/Et$_2$O = 5/1). White solid. Mp = 73-74 °C. $^1$H NMR (CDCl$_3$, 399.78 MHz) $\delta$ 1.25 (brs, 21H), 7.53 (dd, $J$ = 8.2, 4.1 Hz, 1H), 7.60 (dd, $J$ = 7.8, 7.8 Hz, 1H), 7.68 (d, $J$ = 8.7 Hz, 1H), 7.77 (d, $J$ = 8.7 Hz, 1H), 7.87 (dd, $J$ = 7.8, 1.4 Hz, 1H), 8.03 (dd, $J$ = 7.8, 1.4 Hz, 1H), 8.15 (dd, $J$ = 8.2, 1.8 Hz, 1H), 9.01 (dd, $J$ = 4.1, 1.8 Hz, 1H); $^{13}$C NMR (CDCl$_3$, 100.53 MHz) $\delta$ 111.23, 18.57, 94.55, 106.04, 121.54, 122.08, 124.65, 128.04, 128.67, 129.47, 133.98, 135.57, 142.26, 149.42, 157.46; IR (neat) 3062 m, 2943 s, 2864 s, 2151 m, 1587 m, 1462 s, 1423 m, 1209 w, 993 m, 883 m, 841 m, 758 s, 675 s; MS m/z (relative intensity, %) 360 (11), 359 (M$^+$, 36), 358 (19), 318 (17), 317 (61), 316 (100), 274 (11), 232 (10), 230 (23), 206 (26). HRMS Calcd for C$_{24}$H$_{29}$NSi: 359.2069; Found: 359.2067.
2-(2-((Triisopropylsilyl)ethynyl)phenyl)pyridine (10).

![Structure](image)

The alkynylated product was isolated by GPC. 26% yield. R_f 0.19 (hexane/Et_2O = 5/1). Colorless oil. ^1^H NMR (CDCl_3, 399.78 MHz) δ 1.04-1.05 (m, 21H), 7.23-7.26 (m, 1H), 7.35 (ddd, J = 7.8, 7.3, 1.4 Hz, 1H), 7.43 (ddd, J = 7.8, 7.3, 1.4 Hz, 1H), 7.62 (dd, J = 7.8, 1.4 Hz, 1H), 7.69 (ddd, J = 7.3, 1.4 Hz, 1H), 7.75 (dd, J = 7.3, 1.4 Hz, 1H), 8.00-8.02 (m, 1H) 8.70-8.71 (m, 1H); ^13^C NMR (CDCl_3, 100.53 MHz) δ 10.93, 18.22, 98.59, 102.73, 117.13, 119.51, 121.49, 122.08, 122.79, 127.22, 127.80, 131.63, 133.14, 134.27, 135.08, 136.16, 138.71, 140.60, 148.26, 164.74; IR (neat) 3062 m, 2943 s, 2864 s, 2151 m, 1587 m, 1462 s, 1423 m, 1209 w, 993 m, 883 m, 841 m, 758 s, 675 s; MS m/z (relative intensity, %) 335 (M^+, 3), 294 (15), 293 (54), 292 (100), 250 (10), 206 (17), 182 (10). HRMS Calcd for C_{22}H_{29}NSi: 335.2069; Found: 335.2073.

2-(2,6-Bis((triisopropylsilyl)ethynyl)phenyl)pyridine (11).

The general procedure was applied to 9 except that 3 equivalents of 2 (240 mg, 0.90 mmol) and CsOPiv (220 mg, 0.90 mmol) were used. 64% yield. R_f 0.18 (hexane/EtOAc = 50/1). White solid. Mp = 82-83 °C. ^1^H NMR (CDCl_3, 399.78 MHz) δ 0.92 (brs, 42H), 7.20 (ddd, J = 7.3, 5.1, 0.9 Hz, 1H), 7.28 (t, J = 7.8 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 7.8 Hz, 2H), 7.68 (ddd, J = 7.8, 7.8, 1.8 Hz, 1H), 8.65 (dd, J = 5.1, 0.9 Hz, 1H); ^13^C NMR (CDCl_3, 100.53 MHz) δ 11.03, 18.45, 94.64, 104.76, 122.08, 123.20, 124.82, 127.61, 132.67, 135.61, 145.78, 149.12, 157.85; IR (KBr) 3062 w, 2941 s, 2862 s, 2152 w, 2864 s, 2152 m, 1589 m, 1568 m, 1462 s, 1419 m, 987 m, 881 s, 675 s; MS m/z (relative intensity, %) 515 (M^+, 10), 475 (10), 474 (32), 473 (77), 472 (100), 158 (10), 151 (13). HRMS Calcd for C_{33}H_{49}NSi_2: 515.3404; Found: 515.3401.

3-Methyl-2-(2-((triisopropylsilyl)ethynyl)phenyl)pyridine (13).
65% yield. R<sub>f</sub> 0.27 (hexane/EtOAc = 5/1). White solid. Mp = 44-45 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 399.78 MHz) δ 0.91 (brs, 21H), 2.21 (s, 3H), (dd, <i>J</i> = 7.6, 4.9 Hz, 1H), 7.29-7.42 (m, 3H), 7.51-7.58 (m, 2H), 8.47 (dd, <i>J</i> = 4.9, 1.2 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100.53 MHz) δ 11.09, 18.44, 19.07, 93.47, 105.16, 122.41, 122.54, 127.63, 128.47, 128.53, 132.03, 132.56, 137.49, 143.65, 146.51, 158.61; IR (KBr) 3345 m, 3057 m, 2943 s, 2864 s, 2146 m, 1678 s, 1523 s, 1425 m, 1385 m, 1327 m, 1221 m, 885 m, 823 m; MS <i>m/z</i> (relative intensity, %) 349 (M<sup>+</sup>, 1), 308 (13), 307 (47), 306 (100), 264 (13), 220 (22), 117 (12). HRMS Calcd for C<sub>23</sub>H<sub>31</sub>NSi: 349.2226; Found: 349.2223.

2-(4-Methoxy-2-((triisopropylsilyl)ethynyl)phenyl)-3-methylpyridine (15).

66% yield. R<sub>f</sub> 0.29 (hexane/EtOAc = 3/1). White solid. Mp = 65-66 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 399.78 MHz) δ 0.93 (brs, 21H), 2.23 (s, 3H), 3.87 (s, 3H), 6.98 (dd, <i>J</i> = 8.4, 2.7 Hz, 1H), 7.08 (d, <i>J</i> = 2.7 Hz, 1H), 7.17 (dd, <i>J</i> = 7.8, 4.8 Hz, 1H), 7.24 (d, <i>J</i> = 8.4 Hz, 1H), 7.53 (d, <i>J</i> = 7.8 Hz, 1H), 8.48 (dd, <i>J</i> = 4.8, 1.0 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100.53 MHz) δ 11.09, 18.44, 19.18, 55.44, 93.29, 105.16, 115.11, 116.90, 122.24, 123.49, 129.81, 132.37, 136.53, 137.44, 146.48, 158.41, 158.73; IR (KBr) 3012 w, 2958 s, 2862 s, 2152 w, 1604 s, 1560 m, 1493 m, 1458 m, 1288 s, 1161 m, 1018 m, 879 s, 823 m, 796 m, 679 s; MS <i>m/z</i> (relative intensity, %) 379 (M<sup>+</sup>, 5), 338 (16), 337 (54), 336 (100). HRMS Calcd for C<sub>24</sub>H<sub>33</sub>NOSi: 379.2331; Found: 379.2330.

N,N-Dimethyl-4-(3-methyl-2-pyridinyl)-3-((triisopropylsilyl)ethynyl)aniline (17).

The general procedure was applied to 16 except that the reaction was run at 90 °C.
48% yield. R<sub>f</sub> 0.20 (hexane/Et<sub>2</sub>O = 1/1). Pale yellow solid. Mp = 82-83 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 399.78
MHz) δ 0.92 (brs, 21H), 2.24 (s, 3H), 2.99 (s, 6H), 6.78 (dd, J = 8.5, 2.7 Hz, 1H), 6.88 (d, J = 2.7 Hz, 1H), 7.12 (dd, J = 7.5, 4.6 Hz, 1H), 7.17 (d, J = 8.5 Hz, 1H), 7.49 (d, J = 7.5 Hz, 1H), 8.47 (d, J = 4.6 Hz, 1H); 13C NMR (CDCl3, 100.53 MHz) δ 11.14, 18.47, 19.33, 40.54, 91.84, 106.32, 113.02, 115.76, 121.87, 122.83, 129.37, 132.26, 132.55, 137.30, 146.38, 149.73, 159.02; IR (KBr) 3043 w, 2941 s, 2145 m, 663 m; MS m/z (relative intensity, %) 392 (M+, 2), 351 (13), 350 (46), 349 (100), 263 (10), 146 (10), 139 (10). HRMS Calcd for C25H36N2Si: 392.2648; Found: 392.2651.

**N-Methyl-N-(4-(3-methyl-2-pyridinyl)-3-((triisopropylsilyl)ethynyl)phenyl)acetamide (19).**

![Chemical Structure](image)

74% yield. Rf 0.34 (EtOAc). Pale yellow solid. Mp = 157-158 °C. 1H NMR (CDCl3, 399.78 MHz) 0.92 (brs, 21H), 1.96 (s, 3H), 2.24 (s, 3H), 3.30 (s, 3H), 7.20-7.25 (m, 2H), 7.35-7.40 (m, 2H), 7.56 (d, J = 7.8 Hz, 1H), 8.49 (d, J = 4.1 Hz, 1H); 13C NMR (CDCl3, 100.53 MHz) δ 11.04, 18.42, 19.05, 22.59, 37.14, 95.46, 124.20, 127.13, 130.23, 130.88, 131.98, 137.71, 143.13, 144.02, 146.70, 157.54, 170.48; IR (KBr) 3037 w, 2943 s, 2866 w, 1730 s, 1720 s, 1666 s, 1464 s, 1379 s, 1373 s, 987 s, 887 s; MS m/z (relative intensity, %) 420 (M+, 3), 379 (19), 378 (61), 377 (100). HRMS Calcd for C26H36N2OSi: 420.2597; Found: 420.2600.

**Methyl 4-(3-methylpyridin-2-yl)-3-((triisopropylsilyl)ethynyl)benzoate (21).**

![Chemical Structure](image)

68% yield. Rf 0.27 (hexane/EtOAc = 3/1). Colorless oil. Bp = 160 °C (1.5 mmHg). 1H NMR (CDCl3, 399.78 MHz) δ 0.92 (brs, 21H), 2.20 (s, 3H), 3.96 (s, 3H), 7.21 (dd, J = 7.8, 5.0 Hz, 1H), 7.40 (d, J = 7.8 Hz, 1H), 7.55 (dd, J = 7.8, 0.9 Hz, 1H), 8.06 (dd, J = 7.8, 1.8 Hz, 1H), 8.23 (d, J = 1.8 Hz, 1H), 8.49 (d, J = 5.0, 0.9 Hz, 1H); 13C NMR (CDCl3, 100.53 MHz) δ 11.04, 18.43, 18.91, 52.33, 94.90, 103.98, 122.80, 123.10, 128.95, 129.40, 131.98, 133.75, 137.70, 146.65, 147.76, 157.65, 166.32; IR (KBr) 3047 m, 2866 s, 2156 s, 1730 s, 1573 s, 1370 s, 1464 s, 1373 s, 987 s, 887 s; MS m/z (relative intensity, %) 407 (M+, 1), 366 (14), 365 (50), 364 (100), 322 (10), 278 (11). HRMS Calcd for C25H33NO2Si: 407.2281; Found: 407.2280.
2-(4-Acetyl-3-((triisopropylsilyl)ethynyl)phenyl)-3-methylpyridine (23).

The general procedure was applied to 22 except that the reaction was run at 90 °C. 57% yield. Rf 0.29 (hexane/EtOAc = 2/1). Colorless oil. Bp = 160 °C (1.5 mmHg). $^1$H NMR (CDCl$_3$, 399.78 MHz) $\delta$ 0.93 (brs, 21H), 2.20 (s, 3H), 2.66 (s, 3H), 7.21 (dd, $J = 7.8, 4.3$ Hz, 1H), 7.42 (d, $J = 8.0$ Hz, 1H), 7.56 (dd, $J = 7.8, 0.9$ Hz, 1H), 7.99 (dd, $J = 8.0, 1.8$ Hz, 1H), 8.14 (d, $J = 1.8$ Hz, 1H), 8.49 (d, $J = 4.3$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 100.53 MHz) $\delta$ 11.03, 18.42, 18.90, 26.76, 95.06, 103.99, 122.82, 123.26, 128.08, 129.15, 131.86, 132.52, 136.37, 137.70, 146.67, 147.92, 157.57, 197.29; IR (neat) 3047 w, 2945 s, 2866 s, 2156 m, 1689 s, 1574 m, 1464 m, 1398 m, 1358 m, 1286 m, 1240 m, 887 m, 793 m, 737 m, 677 s; MS m/z (relative intensity, %) 391 (M$^+$, 1), 350 (18), 349 (60), 348 (100), 306 (13), 262 (14). HRMS C$_{25}$H$_{33}$NOSi: 391.2331; Found: 391.2329.

2-(4-Fluoro-2-((triisopropylsilyl)ethynyl)phenyl)-3-methylpyridine (25).

62% yield. Rf 0.27 (hexane/EtOAc = 5/1). Colorless oil. Bp = 115 °C (1 mmHg). $^1$H NMR (CDCl$_3$, 399.78 MHz) $\delta$ 0.91-0.95 (m, 21H), 2.21 (s, 3H), 7.11 (ddd, $J = 8.7, 8.3, 2.8$ Hz, 1H), 7.18 (dd, $J = 7.8, 5.0$ Hz, 1H), 7.25-7.29 (m, 2H), 7.53 (d, $J = 8.3$ Hz, 1H), 8.47 (dd, $J = 5.0, 1.1$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 100.53 MHz) $\delta$ 11.03, 18.40, 19.06, 94.93, 103.85, 115.85 (d, $J = 22.0$ Hz), 119.01 (d, $J = 23.0$ Hz), 122.59, 124.36 (d, $J = 9.5$ Hz), 130.37 (d, $J = 8.6$ Hz), 132.22, 137.60, 139.86, 146.59, 157.67, 161.75 (d, $J = 246.3$ Hz); IR (neat) 3049 m, 2943 s, 2866 s, 2154 s, 1604 s, 1576 s, 1496 s, 1464 s, 1429 s, 1404 s, 1385 m, 1263 s, 1151 s, 1097 s, 960 s, 879 s; MS m/z (relative intensity, %) 367 (M$^+$, 1), 326 (13), 325 (48), 324 (100), 282 (14), 238 (22). HRMS Calcd for C$_{23}$H$_{30}$FNSi: 367.2132; Found: 367.2133.

2-(2-((Triisopropylsilyl)ethynyl)-1-naphthalenyl)pyridine (27).
The general procedure was applied to 26 except that the reaction was run at 90 °C. 
48% yield. Rf 0.22 (hexane/Et2O = 7/1). Colorless oil. Bp = 160 °C (1 mmHg). 1H NMR (CDCl3, 
399.78 MHz) δ 0.96 (brs, 1H), 7.32-7.63 (m, 5H), 7.78-7.86 (m, 3H), 8.78 (d, J = 5.5 Hz, 1H); 13C 
NMR (CDCl3, 100.53 MHz) δ 11.12, 18.52, 94.92, 106.15, 120.31, 122.20, 126.11 (two overlapping 
peaks), 126.41, 126.75, 127.92, 128.14, 129.01, 131.73, 133.08, 136.08, 141.54, 149.41, 157.95; IR 
(neat) 3057 m, 2864 s, 2144 s, 1589 s, 1564 m, 1466 s, 1383 m, 1236 m, 995 s, 883 s, 820 s, 750 s; 
MS m/z (relative intensity, %) 385 (M+, 6), 344 (21), 343 (61), 342 (100), 300 (10), 256 (17), 142 
(14). HRMS Calcd for C26H31NSi: 385.2226; Found: 385.2228.

2-(3-((Triisopropylsilyl)ethynyl)-2-thiophenyl)pyridine (29).

VII. Procedure for Ruthenium-catalyzed Direct Alkynylation of 4,6-Diarylpyrimidine 30 with 2 
(Scheme 2).

To an oven-dried 5 mL screw-capped vial, 4,6-bis(4-fluorophenyl)pyrimidine 30 (81 mg, 0.30 mmol), 
(bromoethynyl)triisopropylsilane 2 (240 mg, 0.90 mmol), [RuCl2(p-cymene)]2 (9.0 mg, 0.015 mmol), 
CsOPiv (210 mg, 0.90 mmol) and toluene (1.0 mL) were added under a gentle stream of nitrogen. 
The mixture was stirred for 15 h at 100 °C followed by cooling. The mixture was diluted with
EtOAc (10 mL) and washed with NaOH aq. (1 M, 2 × 10 mL). The aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluent: hexane/Et₂O = 30/1) to afford a mixture of 31 and 32 as a pale brown oil. Each of the alkynylated products was isolated by GPC (31: 95 mg, 50 %, 32: 28 mg, 11%). Spectroscopic data are as follows.

**4-(4-Fluoro-2,6-bis((triisopropylsilyl)ethynyl)phenyl)-6-(4-fluorophenyl)pyrimidine (31).**

![Chemical structure](image)

50% yield. Rₜ 0.12 (hexane/Et₂O = 30/1). Colorless oil. ¹H NMR (CDCl₃, 399.78 MHz) δ 0.87 (brs, 21H), 7.17-7.21 (m, 2H), 7.26-7.28 (m, 2H), 7.80 (d, J = 1.4 Hz, 1H), 8.05-8.09 (m, 2H), 9.28 (d, J = 1.4 Hz, 1H); ¹³C NMR (CDCl₃, 100.53 MHz) δ 10.90, 18.31, 97.55, 102.85, 115.94 (d, J = 22.0 Hz), 117.96, 119.71 (d, J = 23.0 Hz), 124.71 (d, J = 10.5 Hz), 129.24 (d, J = 8.6 Hz), 132.89, 139.97, 158.84, 161.67 (d, J = 250.2 Hz), 162.95, 164.60 (d, J = 251.1 Hz), 165.69; IR (neat) 3078 m, 2945 s, 2866 s, 2162 m, 1585 s, 1466 s, 1444 s, 1230 s, 1134 s, 1011 s, 883 s, 843 s, 677 s; MS m/z (relative intensity, %) 628 (M⁺, 17), 587 (27), 586 (63), 585 (70), 546 (16), 545 (45), 544 (100), 543 (10), 243 (11), 215 (20), 208 (19). HRMS Calcd for C₃₈H₅₀F₂N₂Si₂: 628.3481; Found: 628.3486.

**4-(4-Fluoro-2,6-bis((triisopropylsilyl)ethynyl)phenyl)-6-(4-fluoro-2-((triisopropylsilyl)ethynyl)phenyl)pyrimidine (32).**

![Chemical structure](image)

11% yield. Rₜ 0.12 (hexane/Et₂O = 30/1). Colorless oil. ¹H NMR (CDCl₃, 399.78 MHz) δ 0.87-0.95 (brs, 63H), 7.18-7.33 (m, 4H), 8.20 (dd, J = 8.7, 6.0 Hz, 1H), 8.81 (d, J = 1.4 Hz, 1H), 9.33 (d, J = 1.4 Hz, 1H); ¹³C NMR (CDCl₃, 100.53 MHz) δ 10.95, 11.14, 18.31, 18.51, 97.41, 99.14, 103.10 (d, J = 2.9 Hz), 104.30 (d, J = 1.9 Hz), 116.49 (d, J = 22.1 Hz), 120.06 (d, J = 22.1 Hz), 121.38, 121.59 (d, J = 23.0 Hz), 123.79 (d, J = 9.5 Hz), 125.17 (d, J = 10.6 Hz), 132.27 (d, J = 8.6 Hz), 134.09 (d, J =
2.9 Hz), 139.21 (d, J = 3.9 Hz), 158.50, 161.67 (d, J = 250.2 Hz), 164.16; IR (neat) 2944 s, 2866 s, 2158 w, 1585 s, 1518 m, 1464 s, 1442 m, 1134 m, 1009 m, 995 m, 883 s, 675 s; MS-FAB m/z (relative intensity, %) 809 (M+H+, 68), 808 (15), 807 (17), 609 (13), 157 (16), 136 (10), 115 (46), 87 (54), 85 (16), 71 (10), 59 (100), 45 (10). HRMS-FAB Calcd for C₄₉H₇₁F₂N₂Si₃ (M+H+): 809.4888; Found: 809.4882.

VIII. Synthesis of Pentacyclic Heteroarene 36 via Sequential Direct Alkynylation/Desilylative Cyclization (Scheme 3).

To an oven-dried 5 mL screw-capped vial, 2-(1-naphthalenyl)-1H-benzimidazole 34 (61 mg, 0.30 mmol), (bromoethynyl)triisopropylsilane 2 (120 mg, 0.45 mmol), [RuCl₂(μ-cymene)]₂ (9.0 mg, 0.015 mmol), CsOΠv (110 mg, 0.45 mmol) and toluene (1.0 mL) were added under a gentle stream of nitrogen. The mixture was stirred for 15 h at 100 °C followed by cooling. The mixture was diluted with EtOAc (10 mL) and washed with NaOH aq. (1 M, 2 × 10 mL). The aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: hexane/EtOAc = 5/1) to afford the corresponding alkynylated product 35 (77 mg, 72%). Spectroscopic data are as follows.

2-(2-((Triisopropylsilyl)ethynyl)-1-naphthalenyl)-1H-benzo[d]imidazole (35).

72% yield. Rf 0.28 (hexane/EtOAc = 5/1). Pale brown solid. Mp = 99-100 °C. ¹H NMR (CDCl₃, 399.78 MHz) δ 0.93-0.97 (m, 21H), 7.31-7.35 (m, 2H), 7.46-7.55 (m, 3H), 7.64 (d, J = 8.7 Hz, 1H), 7.85-7.90 (m, 3H), 8.42-8.44 (m, 1H), 9.83 (brs, 1H); ¹³C NMR (CDCl₃, 100.53 MHz) δ 11.09, 18.46, 96.84, 105.80, 121.15, 122.57, 122.72, 126.60, 127.05, 127.70, 127.89, 129.02 (two overlapping peaks), 129.78, 130.79, 131.87, 133.06, 148.91; IR (KBr) 3059 m, 2943 s, 2864 s, 2146 m, 1592 m, 1504 m, 1456 s, 1414 s, 1275 m, 1227 m, 997 m, 908 s, 883 s, 820 m, 746 s, 677 s; MS m/z (relative intensity, %) 424 (M⁺, 19), 383 (20), 382 (65), 381 (100), 295 (11), 271 (12). HRMS Calcd for C₂₉H₂₂N₂Si: 424.2335; Found: 424.2331.

Procedure for the Desilylative Cyclization of 35.

Alkynylated arene 35 (53 mg, 0.13 mmol) was dissolved in THF (3.0 mL). TBAF (1.0 M in THF,
0.13 mL, 0.13 mmol) was then added. The resulting solution was stirred at room temperature. After 1 h, the reaction system was quenched with H2O (20 mL). The mixture was extracted with Et2O (3 × 15 mL) and the combined organic layers were washed with brine (15 mL), dried over MgSO4, filtered and evaporated *in vacuo*. The obtained crude product was purified by column chromatography (eluent: hexane/EtOAc = 7/1) to afford the desired pentacyclic heteroarene 36 (yellow solid, 19 mg, 55%). Spectroscopic data are as follows.

**Benzimidazo[2,1-a]benz[h]isoquinoline (36).**

\[
\begin{align*}
\text{55% yield. R}_{f} & \, 0.21 \text{ (hexane/EtOAc = 7/1). Yellow solid. Mp} = 233-234 \, ^{\circ}\text{C.} \\
\text{H NMR (CDCl}_3, \, 399.78 \text{ MHz}) & \, \delta \, 5.74-5.78 \, (m, \, 2H), \, 7.30-7.38 \, (m, \, 2H), \, 7.60-7.80 \, (m, \, 4H), \, 7.90-7.97 \, (m, \, 3H), \, 9.01 \, (d, \, J = 8.3 \, Hz, \, 1H); \\
\text{C NMR (CDCl}_3, \, 100.53 \text{ MHz}) & \, \delta \, 94.81, \, 110.41, \, 118.13, \, 121.08, \, 122.97, \, 124.00, \, 124.29, \, 125.55, \, 127.37, \, 127.41, \, 128.11, \, 128.30, \, 130.44, \, 130.78, \, 134.06, \, 137.07, \, 138.59, \, 149.35, \, 157.43; \\
\text{IR (KBr)} & \, 3057 \, m, \, 2962 \, m, \, 1747 \, w, \, 1653 \, w, \, 1547 \, m, \, 1521 \, m, \, 1450 \, m, \, 1402 \, m, \, 1336 \, m, \, 1257 \, s, \, 1095 \, m, \, 1016 \, m, \, 816 \, s, \, 748 \, s, \, 727 \, s; \\
\text{MS m/z (relative intensity, %)} & \, 269 \, (29), \, 268 \, (M^+, \, 100), \, 267 \, (30). \\
\text{HRMS Calcd for C}_{19}H_{12}N_{2}: \, 268.1000; \, \text{Found:} \, 268.0999.
\end{align*}
\]