Salicylic Acids as Readily Available Starting Materials for the Synthesis of meta-Substituted Biaryls

Supporting Information

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General experimental information

All chemicals used in this work were purchased from commercial sources and used without further purification, except 5-iodo-1-tosyl-1H-indole and 4-acetamido-2-hydroxybenzoic acid that were prepared following literature procedures. Analytical thin-layer chromatography was performed on pre-coated Merk silica gel F$_{254}$ plates and visualized under a UV light. Melting points were obtained using a Bibby Stuart Scientific apparatus and are uncorrected. IR spectra were recorded using a Bruker Tensor 37 FTIR machine and are quoted in cm$^{-1}$. $^1$H NMR spectra, recorded at 400 MHz, are referenced to the residual solvent peak at 7.26 ppm (CDCl$_3$) and 2.05 ppm (acetone-d$_6$). $^{13}$C NMR spectra, recorded at 101 MHz, are referenced to the residual solvent peak at 77.0 ppm (CDCl$_3$) and 29.8 ppm (acetone-d$_6$).
Optimization tables

*Table 1. Systematic screening of reaction conditions.*

![Chemical structure](image)

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<th>Entries</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>AcOH (equiv)</th>
<th>Pd(OAc)$_2$ (mol%)</th>
<th>Yield of 3a (%)</th>
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*Unless otherwise noted, all reactions were carried out using 1.0 equiv of 1a, 3.0 equiv of 2a and 1.0 equiv of silver carbonate, yields were determined by $^1$H NMR analysis using mesitylene as an internal standard.

$^b$ 200 μL of DMSO were also added.

$^c$ 5.0 equiv of water were also added.
Table 2. Palladium catalysts screening.\textsuperscript{a}

![Reaction scheme](image1)

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<td>17</td>
<td>PEPPSI-IPr</td>
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<td>Pd(PPh\textsubscript{3})\textsubscript{3}</td>
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\textsuperscript{a} Unless otherwise noted, all reactions were carried out using 1.0 equiv of 1\textsubscript{a}, 3.0 equiv of 2\textsubscript{a}, 1.0 equiv of silver carbonate and 200 µL (7.0 equiv) of acetic acid for 16 h at the temperature of 130 °C, yields were determined by \textsuperscript{1}H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

\textsuperscript{b} 1 mol\% of Pd\textsubscript{2}(dba)\textsubscript{3} was used.

\textsuperscript{c} 2 mol\% of IMesCl were also added.

\textsuperscript{d} 2 mol\% of IPrCl were also added.

Table 3. Silver salts screening.\textsuperscript{a}

![Reaction scheme](image2)

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\textsuperscript{a} Unless otherwise noted, all reactions were carried out using 1.0 equiv of 1\textsubscript{a}, 3.0 equiv of 2\textsubscript{a}, 2 mol\% of Pd(OAc)\textsubscript{2}, 200 µL (7.0 equiv) of acetic acid, ran for 16 h at 130 °C, yields were determined by \textsuperscript{1}H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

\textsuperscript{b} 0.5 equiv of silver oxide were used in the reaction.

Table 4. Solvent screening.\textsuperscript{a}
Unless otherwise noted, all reactions were carried out using 1.0 equiv of 1a, 3.0 equiv of 2a, 2 mol% of PEPPSI-IPr, ran for 16 h at the temperature of 130 °C, yields were determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

Table 5. Optimization of the formal meta-arylation using PEPPSI-IPr

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<th>Entries</th>
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<th>Ag₂CO₃ (equiv)</th>
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*Unless otherwise noted, all reactions were carried out using 1.0 equiv of 1a, 3.0 equiv of 2a, 2 mol% of PEPPSI-IPr, ran for 16 h, yields were determined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

ᵇ 0.5 equiv of K₂CO₃ were used in the reaction.
ᶜ 0.5 equiv of Cs₂CO₃ were used in the reaction.
3',5'-Dimethyl-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 ºC for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 3',5'-dimethyl-[1,1'-biphenyl]-3-ol (3aa) as a light orange oil (80.0 mg, 81%). ¹H NMR (400 MHz, CDCl₃) δ 7.29 (t, J = 7.9 Hz, 1H), 7.20 (s, 2H), 7.17-7.15 (m, 1H), 7.07-7.05 (m, 1H), 7.01 (s, 1H), 6.90 (ddd, J = 8.0, 2.6, 0.9 Hz, 1H), 4.76 (s, 1H), 2.38 (s, 6H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 155.7, 143.3, 140.8, 138.3, 129.9, 129.1, 125.1, 119.9, 114.1, 114.0, 21.4 ppm. These data are consistent with those previously reported.²

4-Fluoro-3',5'-dimethyl-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), 3-fluoro-2-hydroxybenzoic acid (78.1 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (1.0 mL) was heated at 160 ºC for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 4-fluoro-3',5'-dimethyl-[1,1'-biphenyl]-3-ol (3ab) as a light orange oil (81.1 mg, 75%). ¹H NMR (400 MHz, CDCl₃) δ 7.22 (dd, J = 8.5, 2.2 Hz, 1H), 7.15 (s, 2H), 7.14-7.09 (m, 1H), 7.06-7.04 (m, 1H), 6.99 (s, 1H), 5.17 (s, 1H), 2.37 (s, 6H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 150.6 (d, J = 237.4 Hz), 143.5 (d, J = 14.6 Hz), 140.1, 138.7 (d, J = 3.6 Hz), 138.3, 129.1, 125.0, 119.5 (d, J = 6.4 Hz), 116.0 (d, J = 1.8 Hz), 115.5 (d, J = 18.3 Hz), 21.4 ppm. These data are consistent with those previously reported.²

3',4,5'-Trimethyl-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), 2-hydroxy-3-methylbenzoic acid (76.1 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (1.0 mL) was heated at 160 ºC for 16 h. After this time, the reaction mixture was filtered
through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 3',4,5'-trimethyl-[1,1'-biphenyl]-3-ol (3ac) as an orange oil (75.3 mg, 71%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.18-7.16 (m, 3H), 7.08 (dd, J = 7.7, 1.7 Hz, 1H), 7.01-7.00 (m, 1H), 6.98 (s, 1H), 4.69 (s, 1H), 2.37 (s, 6H), 2.29 (s, 3H) ppm. \(^13\)C NMR (101 MHz, CDCl\(_3\)) δ 153.9, 140.8, 140.8, 138.2, 131.2, 128.8, 124.9, 122.5, 119.6, 113.7, 21.4, 15.4 ppm. These data are consistent with those previously reported.\(^2\)

3',5'-Dimethyl-5-nitro-[1,1'-biphenyl]-3-ol

\[
\begin{align*}
\text{O}_2\text{N} & \quad \text{Me} \\
\text{Me} & \quad \text{Me}
\end{align*}
\]

A mixture of PEPSI-IPr (6.8 mg, 0.010 mmol), Ag\(_2\)CO\(_3\) (69.0 mg, 0.25 mmol), K\(_2\)CO\(_3\) (25.0 mg, 0.18 mmol), 2-hydroxy-4-nitrobenzoic acid (91.6 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 75:25) to afford 3',5'-dimethyl-5-nitro-[1,1'-biphenyl]-3-ol (3ad) as a yellow solid (63 mg, 52%). m. p. 148 ºC. IR: 3424, 3092, 1591, 1343, 745 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 8.04 (dd, J = 2.0, 1.6 Hz, 1H), 7.64 (app. t, J = 2.2 Hz, 1H), 7.38 (dd, J = 2.4, 1.5 Hz, 1H), 7.21 (s, 2H), 7.07 (s, 1H), 5.36 (s, 1H), 2.40 (s, 6H) ppm. \(^13\)C NMR (101 MHz, CDCl\(_3\)) δ 156.3, 149.5, 144.5, 138.8, 138.4, 130.3, 125.0, 120.3, 114.8, 108.9, 21.4 ppm. HRMS: calcd for C\(_{12}\)H\(_{13}\)NO\(_2\), 243.0890 (M\(^+\)); found, 243.0890.

3',5'-Dimethyl-5-(trifluoromethyl)-[1,1'-biphenyl]-3-ol

\[
\begin{align*}
\text{F}_3\text{C} & \quad \text{Me} \\
\text{Me} & \quad \text{Me}
\end{align*}
\]

A mixture of PEPSI-IPr (6.8 mg, 0.010 mmol), Ag\(_2\)CO\(_3\) (69.0 mg, 0.25 mmol), K\(_2\)CO\(_3\) (25.0 mg, 0.18 mmol), 2-hydroxy-4-(trifluoromethyl) benzoic acid (103.1 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 3',5'-dimethyl-5-(trifluoromethyl)-[1,1'-biphenyl]-3-ol (3ae) as a brownish red oil (89.0 mg, 67%). IR: 3350, 2918, 1599, 1120, 699 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.40-7.39 (m, 1H), 7.21-7.20 (m, 1H), 7.18 (s, 2H), 7.04 (s, 2H), 5.08 (s, 1H), 2.39 (s, 6H) ppm. \(^13\)C NMR (101 MHz, CDCl\(_3\)) δ 156.0, 144.2, 139.4, 138.6, 132.3 (q, J = 32.3 Hz), 129.8, 125.0, 123.9 (q, J = 272.4 Hz), 117.4, 116.6 (q, J = 3.9 Hz), 110.9 (q, J = 3.8 Hz), 21.3 ppm. HRMS: calcd for C\(_{15}\)H\(_{15}\)F\(_3\)O, 266.0918 (M\(^+\)); found, 266.0913.
5-Fluoro-3',5'-dimethyl-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), 4-fluoro-2-hydroxybenzoic acid (78.1 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 ºC for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 5-fluoro-3',5'-dimethyl-[1,1'-biphenyl]-3-ol (3af) as a brownish orange solid (73.1 mg, 68%). m. p. 95-96 ºC. IR: 3375, 2917, 1620, 1126, 840 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.16-7.15 (m, 2H), 7.02-7.01 (m, 1H), 6.87 (ddd, J = 9.8, 2.3, 1.5 Hz, 1H), 6.83-6.82 (m, 1H), 6.54 (dt, J = 9.8, 2.3 Hz, 1H), 4.90 (s, 1H), 2.37 (s, 6H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ 163.8 (d, J = 244.9 Hz), 156.8 (d, J = 12.0 Hz), 144.6 (d, J = 9.8 Hz), 139.7 (d, J = 2.6 Hz), 138.4, 129.7, 124.9, 109.9 (d, J = 2.7 Hz), 106.7 (d, J = 22.3 Hz), 101.8 (d, J = 24.9 Hz), 21.36 ppm. HRMS: calcd for C₁₄H₁₃FO, 216.0959 (M⁺); found, 216.0945.

5-Chloro-3',5'-dimethyl-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), 4-chloro-2-hydroxybenzoic acid (86.3 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 160 ºC for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 5-chloro-3',5'-dimethyl-[1,1'-biphenyl]-3-ol (3ag) as a light orange solid (73.3 mg, 63%). ¹H NMR (400 MHz, CDCl₃) δ 7.15-7.14 (m, 3H), 7.02 (s, 1H), 6.93-6.92 (m, 1H), 6.82-6.81 (m, 1H), 4.84 (s, 1H), 2.37 (s, 6H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ 156.3, 144.4, 139.5, 138.4, 135.1, 129.7, 124.9, 120.1, 114.4, 112.6, 21.3 ppm. HRMS: calcd for C₁₄H₁₃ClO, 232.0655 (M⁺); found, 232.0649. These data are consistent with those previously reported.²

5-Bromo-3',5'-dimethyl-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), 4-bromo-2-hydroxybenzoic acid (95.5 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 160 ºC for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 5-bromo-3',5'-dimethyl-[1,1'-biphenyl]-3-ol (3ah) as a red solid (72.8 mg, 66%). m. p. 137-140 ºC. IR: 3375, 2917, 1620, 1126, 840 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.24 (m, 3H), 7.02 (s, 1H), 6.93-6.92 (m, 1H), 6.82-6.81 (m, 1H), 4.84 (s, 1H), 2.37 (s, 6H) ppm.

¹³C NMR (101 MHz, CDCl₃) δ 156.3, 144.4, 139.5, 138.4, 135.1, 129.7, 124.9, 120.1, 114.4, 112.6, 21.3 ppm. HRMS: calcd for C₁₄H₁₃BrO, 234.0500 (M⁺); found, 234.0493. These data are consistent with those previously reported.²
A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), 4-bromo-2-hydroxybenzoic acid (108.5 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 5-bromo-3',5',5'-trimethyl-[1,1'-biphenyl]-3-ol (3ah) as a light yellow solid (92.5 mg, 67%). ¹H NMR (400 MHz, CDCl₃) δ 7.30 (app. t, J = 1.6 Hz, 1H), 7.15 (s, 2H), 7.02 (s, 1H), 6.97 (app. p, J = 2.3 Hz, 2H), 4.83 (s, 1H), 2.37 (s, 6H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 156.4, 144.7, 139.4, 138.4, 129.7, 125.0, 123.0 (CH+C), 117.3, 113.1, 21.4 ppm. These data are consistent with those previously reported.²

3',5,5'-Trimethyl-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), 2-hydroxy-4-methylbenzoic acid (76.1 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 3',5,5'-trimethyl-[1,1'-biphenyl]-3-ol (3ai) as a light orange solid (75.2 mg, 71%). ¹H NMR (400 MHz, CDCl₃) δ 7.18 (s, 2H), 6.99-6.97 (m, 2H), 6.85-6.84 (m, 1H), 6.63 (s, 1H), 4.66 (s, 1H), 2.37 (s, 6H), 2.36 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 155.7, 143.1, 140.9, 139.9, 138.2, 129.0, 125.0, 120.8, 114.8, 111.3, 21.44, 21.37 ppm. These data are consistent with those previously reported.²

N-(5-hydroxy-3',5'-dimethyl-[1,1'-biphenyl]-3-y)acetamide

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), 4-acetamido-2-hydroxybenzoic acid (97.6 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by long column chromatography (hexanes:EtOAc 50:50) to afford N-(5-hydroxy-3',5'-dimethyl-[1,1'-biphenyl]-3-y)acetamido (3aj) as a light brown solid (52 mg, 41%). m. p. 238-240 °C. IR: 3355, 3098, 1746, 1626, 1656, 1592, 1552, 1268, 695 cm⁻¹. ¹H NMR (400 MHz, acetone-d₆) δ 9.09 (s, 1H), 8.35 (s, 1H), 7.37 (s, 1H), 7.28 (s, 1H), 7.17 (s, 2H), 6.98 (s, 1H), 6.79-6.78 (m, 1H), 2.33
(s, 6H), 2.09 (s, 3H) ppm. $^{13}$C NMR (101 MHz, acetone-d$_6$) δ 168.9, 158.9, 143.7, 141.9, 141.9, 138.9, 129.8, 125.5, 109.9, 109.7, 106.1, 24.4, 21.4 ppm. HRMS: calcd for C$_{16}$H$_{17}$NO$_2$, 255.1259 (M$^+$); found, 255.1254.

5-Methoxy-3',5'-dimethyl-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag$_2$CO$_3$ (69.0 mg, 0.25 mmol), 2-hydroxy-4-methoxybenzoic acid (84.1 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 ºC for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 50:50) to afford 5-methoxy-3',5'-dimethyl-[1,1'-biphenyl]-3-ol (3ak) as a brownish orange oil (25.0 mg, 22%). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.17 (s, 2H), 7.00 (s, 1H), 6.71-6.70 (m, 1H), 6.65-6.64 (m, 1H), 6.39 (app. t, $J$ = 2.3 Hz, 1H), 4.83 (s, 1H), 3.84 (s, 3H), 2.37 (s, 6H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 161.1, 156.8, 144.1, 140.8, 138.2, 129.3, 125.0, 106.9, 105.7, 100.3, 55.4, 21.4 ppm. These data are consistent with those previously reported.²

6-Fluoro-3',5'-dimethyl-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag$_2$CO$_3$ (69.0 mg, 0.25 mmol), K$_2$CO$_3$ (25.0 mg, 0.18 mmol), 5-fluoro-2-hydroxybenzoic acid (78.1 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 ºC for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 6-fluoro-3',5'-dimethyl-[1,1'-biphenyl]-3-ol (3an) as an orange solid (58.0 mg, 53%). m. p. 53-54 ºC. IR: 3352, 2916, 1420, 1204, 765 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.15 (s, 2H), 7.03-6.98 (m, 2H), 6.89-6.86 (m, 1H), 6.76-6.72 (m, 1H), 4.70 (s, 1H), 2.37 (s, 6H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 154.4 (d, $J$ = 239.9 Hz), 151.6 (d, $J$ = 2.3 Hz), 138.1, 135.6 (d, $J$ = 1.4 Hz), 130.3 (d, $J$ = 15.5 Hz), 129.7, 126.9 (d, $J$ = 2.9 Hz), 117.1 (d, $J$ = 3.5 Hz), 116.9 (d, $J$ = 25.1 Hz), 115.1 (d, $J$ = 8.1 Hz), 21.5 ppm. HRMS: calcd for C$_{14}$H$_{13}$FO, 216.0950 (M$^+$); found, 216.0945.

4'-Nitro-[1,1'-biphenyl]-3-ol
A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol) and 1-iodo-4-nitrobenzene (374.0 mg, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 75:25) to afford 4'-nitro-[1,1'-biphenyl]-3-ol (3ba) as a yellow solid (64.5 mg, 60%). ¹H NMR (400 MHz, acetone-d₆) δ 8.61 (s, 1H), 8.36-8.32 (m, 2H), 7.94-7.91 (m, 2H), 7.38 (t, J = 7.9 Hz, 1H), 7.27-7.23 (m, 2H), 6.98 (ddd, J = 8.1, 2.4, 0.9 Hz, 1H) ppm. ¹³C NMR (101 MHz, acetone-d₆) δ 159.0, 148.3, 148.1, 141.0, 131.2, 128.7, 124.8, 119.5, 116.8, 115.0 ppm. These data are consistent with those previously reported.²

**4’-(Trifluoromethyl)-[1,1’-biphenyl]-3-ol**

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 4-iodobenzotrifluoride (220 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 4’-(trifluoromethyl)-[1,1’-biphenyl]-3-ol (3ca) as a pale yellow solid (79.5 mg, 67%). m. p. 73-75 °C. IR: 3261, 1573, 1322, 840 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.73-7.68 (m, 4H), 7.37 (t, J = 7.9 Hz, 1H), 7.21 (ddd, J = 7.7, 1.6, 0.9 Hz, 1H), 7.11-7.10 (m, 1H), 6.91 (ddd, J = 8.1, 2.5, 0.9 Hz, 1H), 4.91 (s, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 156.0, 144.2, 141.6, 130.3, 129.6 (q, J = 32.5 Hz), 124.3 (q, J = 272.0 Hz), 127.4, 125.7 (q, J = 3.8 Hz), 119.9, 115.1, 114.3 ppm. HRMS: calcd for C₁₃H₉F₃O, 238.0605 (M⁺); found, 238.0600.

**4’-Fluoro-[1,1’-biphenyl]-3-ol**

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 1-fluoro-4-iodobenzene (173 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 4’-fluoro-[1,1’-biphenyl]-3-ol (3da) as an off white solid (64.9 mg, 69%). ¹H NMR (400 MHz, CDCl₃) δ 7.56-7.50 (m, 3H), 7.02-7.01 (m, 1H), 6.82 (ddd, J = 8.1, 2.5, 0.9 Hz, 1H), 4.83 (bs, 1H)
C NMR (101 MHz, CDCl$_3$) δ 162.6 (d, $J = 246.6$ Hz), 155.9, 142.1, 136.9 (d, $J = 3.2$ Hz), 130.1, 128.7, 128.6, 119.7, 115.6 (d, $J = 21.4$ Hz), 114.1 (d, $J = 18.4$ Hz) ppm. These data are consistent with those previously reported.

4'-Chloro-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag$_2$CO$_3$ (69.0 mg, 0.25 mmol), K$_2$CO$_3$ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 1-chloro-4-iodobenzene (358 mg, 1.5 mmol) in acetic acid (500 µL) was heated at 150 ºC for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 4'-chloro-[1,1'-biphenyl]-3-ol (3ea) as a light orange solid (69.5 mg, 68%). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.51-7.48 (m, 2H), 7.41-7.38 (m, 2H), 7.31 (t, $J = 7.9$ Hz, 1H), 7.13 (ddd, $J = 7.7$, 1.6, 0.9 Hz, 1H), 7.03-7.02 (m, 1H), 6.83 (ddd, $J = 8.1$, 2.5, 0.9 Hz, 1H), 4.85 (s, 1H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 156.0, 141.8, 139.2, 133.6, 130.1, 128.9, 128.4, 119.6, 114.5, 114.0 ppm. These data are consistent with those previously reported.

4'-Bromo-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag$_2$CO$_3$ (69.0 mg, 0.25 mmol), K$_2$CO$_3$ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 1-bromo-4-iodobenzene (424 mg, 1.5 mmol) in acetic acid (500 µL) was heated at 150 ºC for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 4'-bromo-[1,1'-biphenyl]-3-ol (3fa) as a light orange solid (74.7 mg, 60%). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.58-7.54 (m, 2H), 7.45-7.42 (m, 2H), 7.31 (t, $J = 7.9$ Hz, 1H), 7.13 (ddd, $J = 7.7$, 1.6, 0.9 Hz, 1H), 7.03-7.02 (m, 1H), 6.83 (ddd, $J = 8.1$, 2.5, 0.9 Hz, 1H), 4.79 (s, 1H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 156.1, 141.9, 139.2, 132.0, 130.3, 128.8, 121.9, 119.7, 114.7, 114.1 ppm. These data are consistent with those previously reported.

4'-Iodo-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag$_2$CO$_3$ (69.0 mg, 0.25 mmol), K$_2$CO$_3$ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 1,4-diiodobenzene (495 mg, 1.5 mmol) in acetic acid (500
μL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 4'-iodo-[1,1'-biphenyl]-3-ol (3ga) as an orange solid (59.2 mg, 40%). m. p. 123-126 °C. IR: 3335, 1593, 1445, 1388, 1194, 1002, 878, 823, 780, 688 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, J = 8.4 Hz, 2H), 7.33-7.29 (m, 3H), 7.12 (d, J = 7.8 Hz, 1H), 7.02-7.01 (m, 1H), 6.83 (dd, J = 8.0, 2.5 Hz, 1H), 4.84 (s, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 155.9, 141.9, 140.2, 137.9, 130.2, 129.0, 119.6, 114.6, 113.8, 93.3 ppm. HRMS: calcd for C₁₂H₉O, 296.9698 (M+H⁺); found, 296.9771.

4'-Methoxy-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (35.0 mg, 0.25 mmol), salicylic acid (69.1 mg, 0.50 mmol), 1-iodo-4-methoxybenzene (39.1 mg, 0.167 mmol) in acetic acid (500 μL) was heated at 130 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 4'-methoxy-[1,1'-biphenyl]-3-ol (3ha) as an off white solid (27.7 mg, 83%). ¹H NMR (400 MHz, CDCl₃) δ 7.53-7.49 (m, 2H), 7.28 (t, J = 8.0 Hz, 1H), 7.13 (dd, J = 7.7, 1.6, 1.0 Hz, 1H), 7.03-7.02 (m, 1H), 6.99-6.95 (m, 2H), 6.78 (dd, J = 8.0, 2.5, 0.9 Hz, 1H), 4.78 (s, 1H), 3.85 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 159.3, 155.8, 146.2, 133.3, 129.9, 128.1, 119.4, 114.2, 113.7, 113.6, 55.4 ppm. These data are consistent with those previously reported.²

3'-Hydroxy-[1,1'-biphenyl]-4-carbaldehyde

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (35.0 mg, 0.25 mmol), salicylic acid (69.1 mg, 0.50 mmol), 4-iodobenzaldehyde (38.7 mg, 0.167 mmol) in acetic acid (500 μL) was heated at 130 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 80:20) to afford 3'-hydroxy-[1,1'-biphenyl]-4-carbaldehyde (3ia) as a white solid (28.2 mg, 85%). ¹H NMR (400 MHz, acetone-d₆) δ 10.09 (s, 1H), 8.56 (s, 1H), 8.01-7.99 (m, 2H), 7.86-7.84 (m, 2H), 7.34 (app. t, J = 7.7 Hz, 1H), 7.23-7.19 (m, 2H), 6.94-6.91 (m, 1H) ppm. ¹³C NMR (101 MHz, acetone-d₆) δ 192.5, 158.9, 147.6, 142.0, 136.6, 131.1, 130.9, 128.4, 119.4, 116.4, 115.0 ppm. These data are consistent with those previously reported.² (3'-Hydroxy-[1,1'-biphenyl]-4-yl)mEtOAc
A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (35.0 mg, 0.25 mmol), salicylic acid (69.1 mg, 0.50 mmol), 4-iodobenzyl alcohol (39.1 mg, 0.167 mmol) in acetic acid (500 µL) was heated at 130 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 75:25) to afford 3'-hydroxy-[1,1'-biphenyl]-4-carbaldehyde (3ja) as an off white solid (32.3 mg, 80%).¹ H NMR (400 MHz, CDCl₃) δ 7.58-7.55 (m, 2H), 7.43-7.41 (m, 2H), 7.31 (t, J = 7.9 Hz, 1H), 7.16-7.14 (m, 1H), 7.07-7.06 (m, 1H), 6.83 (ddd, J = 8.1, 2.5, 0.9 Hz, 1H), 5.26 (s, 1H), 5.15 (s, 2H), 2.13 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 171.2, 156.0, 142.4, 140.9, 135.1, 130.0, 128.8, 127.3, 119.7, 114.4, 114.1, 66.1, 21.1 ppm. These data are consistent with those previously reported.²

3',5'-Dinitro-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 1-Iodo-3,5-dinitrobenzene (441 mg, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 50:50) to afford 3',5'-dinitro-[1,1'-biphenyl]-3-ol (3ka) as a yellow solid (82.1 mg, 63%). mp 208-210 °C. IR: 3440, 3076, 1522, 1336, 727 cm⁻¹. ¹H NMR (400 MHz, acetone-d₆) δ 8.93 (t, J = 2.1 Hz, 1H), 8.84 (d, J = 2.1 Hz, 2H), 8.70 (s, 1H), 7.44 (t, J = 7.8 Hz, 1H), 7.38 (ddd, J = 7.7, 1.7, 1.1 Hz, 1H), 7.34 (t, J = 2.0 Hz, 1H), 7.04 (ddd, J = 8.0, 2.4, 1.1 Hz, 1H) ppm. ¹³C NMR (101 MHz, acetone-d₆) δ 159.2, 150.0, 145.2, 138.9, 131.6, 127.6, 119.4, 117.8, 117.5, 115.0 ppm. HRMS: calcd for C₁₂H₈N₂O₅, 260.0433 (M⁺); found, 260.0428.

3',5'-Bis(trifluoromethyl)-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 1-Iodo-3,5-bis(trifluoromethyl)benzene (266 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The
crude product was purified by column chromatography (hexanes:EtOAc 85:15) to afford 3',5'-bis(trifluoromethyl)-[1,1'-biphenyl]-3-ol (3ma) as a white solid (97.0 mg, 63%). m. p. 93-94 °C. IR: 3296, 1378, 701 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.99 (s, 2H), 7.86 (s, 1H), 7.38 (t, J = 7.9 Hz, 1H), 7.18 (dd, J = 7.7, 1.6, 0.9 Hz, 1H), 7.08 (t, J = 2.4 Hz, 1H), 6.92 (dd, J = 8.1, 2.5, 0.8 Hz, 1H), 4.96 (s, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 156.2, 142.8, 140.0, 132.1 (q, J = 33.2 Hz), 130.6, 127.2 (d, J = 2.7 Hz), 123.4 (q, J = 272.7 Hz), 121.1 (dt, J = 7.8, 3.8 Hz), 119.8, 115.8, 114.2 ppm. HRMS: calcd for C₁₄H₁₂F₆O, 306.0474 (M⁺); found, 306.0474.

3'-{(Trifluoromethyl)-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 3-iodobenzotrifluoride (216 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 3'-{(trifluoromethyl)-[1,1'-biphenyl]-3-ol (3ma) as an off white solid (80.9 mg, 68%). ¹H NMR (400 MHz, CDCl₃) δ 7.81 (s, 1H), 7.75-7.73 (m, 1H), 7.62-7.53 (m, 2H), 7.34 (t, J = 7.9 Hz, 1H), 7.17 (ddd, J = 7.7, 1.6, 0.9 Hz, 1H), 7.08-7.07 (m, 1H), 6.87 (ddd, J = 8.1, 2.5, 0.9 Hz, 1H), 4.85 (s, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 156.0, 141.5, 131.2 (q, J = 32.2 Hz), 130.4, 130.4, 130.3, 129.2, 124.2 (q, J = 272.4 Hz), 124.2 (q, J = 3.8 Hz), 123.9 (q, J = 3.8 Hz), 119.8, 115.0, 114.2 ppm. These data are consistent with those previously reported.²

1-(3'-Hydroxy-[1,1'-biphenyl]-3-yl)ethanone

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (35.0 mg, 0.25 mmol), salicylic acid (69.1 mg, 0.50 mmol), 3'-idoacetophenone (41.0 mg, 0.167 mmol) in acetic acid (500 µL) was heated at 130 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 80:20) to afford 1-(3'-hydroxy-[1,1'-biphenyl]-3-yl)ethanone (3na) as a light orange oil (27.3 mg, 77%). ¹H NMR (400 MHz, CDCl₃) δ 8.17 (app. t, J = 1.6 Hz, 1H), 7.93 (ddd, J = 7.7, 1.7, 1.2 Hz, 1H), 7.77 (ddd, J = 7.7, 1.9, 1.1 Hz, 1H), 7.53 (t, J = 7.7 Hz, 1H), 7.33 (t, J = 7.9 Hz, 1H), 7.18 (ddd, J = 7.7, 1.6, 1.0 Hz, 1H), 7.12-7.11 (m, 1H), 6.88 (ddd, J = 8.1, 2.5, 0.9 Hz, 1H), 5.34 (s, 1H), 2.66 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 198.5, 156.2, 141.9, 141.3, 137.6, 131.8, 130.2, 129.1, 127.5, 126.9, 119.7, 114.8, 114.2, 26.8 ppm. These data are consistent with those previously reported.²

3'-Methyl-[1,1'-biphenyl]-3-ol
A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (35 mg, 0.25 mmol), salicylic acid (69.1 mg, 0.50 mmol), 3-Iodotoluene (193 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 3'-methyl-[1,1'-biphenyl]-3-ol (3oa) as an orange oil (50.6 mg, 55%). ¹H NMR (400 MHz, CDCl₃) δ 7.40-7.28 (m, 4H), 7.18-7.16 (m, 2H), 7.07-7.06 (m, 1H), 6.82 (ddd, J = 8.0, 2.6, 0.9 Hz, 1H), 4.84 (s, 1H), 2.42 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 155.8, 143.2, 140.7, 138.4, 129.9, 128.7, 128.3, 127.9, 124.2, 119.8, 114.1, 114.1, 21.5 ppm. These data are consistent with those previously reported. ²

2'-Fluoro-[1,1'-biphenyl]-3-ol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 2-fluoriodobenzene (175 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 2'-fluoro-[1,1'-biphenyl]-3-ol (3qa) as a light brown solid (23.0 mg, 24%). m. p. 99-101 °C. IR: 3222, 292, 175, 1571, 1580, 759 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.43 (td, J = 7.7, 1.8 Hz, 1H), 7.34-7.29 (m, 2H), 7.22-7.12 (m, 3H), 7.05-7.03 (m, 1H), 6.85 (ddd, J = 8.1, 2.6, 0.9 Hz, 1H), 4.78 (s, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 159.7 (d, J = 248.0 Hz), 155.5, 137.4, 130.7 (d, J = 3.4 Hz), 129.7, 129.1 (d, J = 8.3 Hz), 128.6 (d, J = 13.3 Hz), 124.3 (d, J = 3.7 Hz), 121.6 (d, J = 2.8 Hz), 116.2 (d, J = 17.6 Hz), 116.0 (d, J = 2.0 Hz), 114.7 ppm. HRMS: calcd for C₁₂H₇FO, 188.0637 (M⁺); found, 188.0632.

3-(1-Tosyl-1H-indol-5-yl)phenol

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag₂CO₃ (69.0 mg, 0.25 mmol), K₂CO₃ (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 5-iiodo-1-tosyl-1H-indole (596 mg, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 70:30) to afford 3-(1-tosyl-1H-indol-5-yl)phenol (3ra) as a brown solid (54.5 mg, 30%). ¹H NMR (400 MHz, CDCl₃) δ 8.02 (d, J = 8.6 Hz, 1H), 7.81-
7.78 (m, 2H), 7.70-7.69 (m, 1H), 7.58 (d, J = 3.7 Hz, 1H), 7.51 (dd, J = 8.6, 1.8 Hz, 1H), 7.29 (t, J = 7.9 Hz, 1H), 7.24-7.22 (m, 2H), 7.16-7.14 (m, 1H), 7.07-7.05 (m, 1H), 6.80 (ddd, J = 8.1, 2.5, 0.9 Hz, 1H), 6.69 (dd, J = 3.7, 0.7 Hz, 1H), 4.91 (s, 1H), 2.34 (s, 3H) ppm. 

13C NMR (101 MHz, CDCl3) δ 155.9, 145.1, 143.1, 136.3, 135.3, 134.3, 131.3, 130.0, 130.0, 127.0, 126.9, 124.1, 120.0, 119.8, 114.3, 114.0, 113.7, 109.3, 21.6 ppm. These data are consistent with those previously reported.2

3-(2,6-Dichloropyridin-4-yl)phenol

![3sa](image)

A mixture of PEPPSI-IPr (6.8 mg, 0.010 mmol), Ag2CO3 (69.0 mg, 0.25 mmol), K2CO3 (25.0 mg, 0.18 mmol), salicylic acid (69.1 mg, 0.50 mmol), 2,6-dichloro-4-iodopyridine (409 µL, 1.5 mmol) in acetic acid (500 µL) was heated at 150 °C for 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 85:15) to afford 3-(2,6-dichloropyridin-4-yl)phenol (3sa) as a pale yellow solid (84.0 mg, 70%). 1H NMR (400 MHz, CDCl3) δ 7.45 (s, 2H), 7.37 (t, J = 7.9 Hz, 1H), 7.17-7.15 (m, 1H), 7.06-7.05 (m, 1H), 6.95 (ddd, J = 8.1, 2.5, 0.9 Hz, 1H) 5.01 (bs, 1H) ppm. 13C NMR (101 MHz, CDCl3) δ 156.4, 153.7, 151.1, 137.4, 130.7, 120.9, 119.5, 117.3, 114.1 ppm. These data are consistent with those previously reported.2
Derivatization of product 3ai

Procedure to prepare 2-((3',5'-dimethyl-[1,1'-biphenyl]-3-yl)methyl)-5-nitropyridine (4a).³

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\text{NaH (11 mg, 0.275 mmol, 60\% in mineral oil) was slowly added to a solution of biaryl 3ai (53.1 mg, 0.25 mmol) in DMF (0.5 mL), at 0 °C. After stirring for 30 min, 2-chloro-5-nitro-pyridine (40.0 mg, 0.25 mmol) was added, and the resulting mixture was stirred at room temperature for 16 h. After that time, the crude mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL), the filtrate was evaporated to dryness, and the crude product was purified by column chromatography (hexanes:EtOAc 85:15) to afford 2-((3',5'-dimethyl-[1,1'-biphenyl]-3-yl)methyl)-5-nitropyridine (4a) as a pale brownish solid (81.0 mg, 97\%). m. p. 93–95 °C. IR: 2916, 1569, 1347, 1300, 1259, 842, 684 cm\(^{-1}\).} 

\[
\text{1H NMR (400 MHz, CDCl}_3\text{): }\delta 9.07 (d, J = 2.8 Hz, 1H), 8.47 (dd, J = 9.1, 2.8 Hz, 1H), 7.33 (s, 1H), 7.19 (s, 2H), 7.16 (s, 1H), 7.04 (d, J = 9.1 Hz, 1H), 7.00 (s, 1H), 6.94 (s, 1H), 2.45 (s, 3H), 2.37 (s, 6H) ppm.} 

\[
\text{13C NMR (101 MHz, CDCl}_3\text{): }\delta 167.1, 153.1, 145.2, 143.4, 140.4, 140.3, 140.2, 138.4, 134.9, 129.4, 125.7, 125.1, 120.5, 117.3, 111.2, 21.6, 21.4 ppm. HRMS: calcd for C\text{\textsubscript{30}}H\text{\textsubscript{29}}N\text{\textsubscript{2}}O\text{\textsubscript{3}}, 335.1317 (M+H\textsuperscript{+}); found, 335.1390.} 

Procedure to prepare 3-methoxy-3',5,5'-trimethyl-1,1'-biphenyl (4b).⁴

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\text{K}_2\text{CO}_3 (32 mg, 0.23 mmol) was added to a solution of biaryl 3ai (21.2 mg, 0.10 mmol) in acetone (0.5 mL). After stirring for 1 min, MeI (14 µL, 0.23 mmol) was added and the resulting mixture was stirred at room temperature for 16 h. After that time, the mixture was filtered through a small plug of silica with EtOAc (4 × 5 mL), the filtrate was evaporated to dryness, and the crude product was purified by column chromatography (hexanes) to afford 3-methoxy-3',5,5'-trimethyl-1,1'-biphenyl (4b) as a colorless oil (21.7 mg, 96\%). IR: 2918, 1590, 1461, 1262, 1152, 1064, 836, 694 cm\(^{-1}\). \text{1H NMR (400 MHz, CDCl}_3\text{): }\delta 7.20 (s, 2H), 7.00 (s, 2H), 6.93 (s, 1H), 6.72 (s, 1H), 3.86 (s, 3H), 2.40 (s, 3H), 2.39 (s, 6H) ppm.} 

\[
\text{13C NMR (101 MHz, CDCl}_3\text{): }\delta 159.9, 142.9, 141.3, 139.6, 138.2, 129.0, 125.1, 120.7, 113.5, 109.9, 55.3, 21.7, 21.4 ppm. HRMS: calcd for C\text{\textsubscript{16}}H\text{\textsubscript{19}}O, 227.1358 (M+H\textsuperscript{+}); found, 227.1430.} 

Procedure to prepare 3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate (4f).\(^5\)

\[
\begin{array}{c}
\text{Me} \hspace{1cm} \text{Me} \hspace{1cm} \text{Me} \\
\text{HO} \hspace{1cm} \text{3ai} \hspace{1cm} \text{TfO} \\
\end{array}
\begin{array}{c}
\text{Pyridine, DCM}
\end{array}
\begin{array}{c}
0 \degree C \rightarrow r.t. \hspace{1cm} 1 \text{ h}
\end{array}
\begin{array}{c}
\text{Me} \hspace{1cm} \text{Me} \hspace{1cm} \text{Me} \\
\text{TfO} \hspace{1cm} \text{4f}
\end{array}
\]

A solution of trifluoromethanesulfonic anhydride (245 µL, 1.44 mmol) in DCM (0.6 mL) was added dropwise to a solution of pyridine (195 µL, 2.4 mmol) and 3ai (254 mg, 1.2 mmol) in anhydrous DCM into an ice bath. After complete addition, the mixture was warmed to room temperature and allowed to stir for 1 h. The mixture was then filtered through a small plug of silica with EtOAc (4 × 5 mL), the filtrate was evaporated to dryness, the crude product was purified by column chromatography (hexanes) to afford 3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate (4f) as a colorless oil (397 mg, 96%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.40\) (s, 1H), 7.26 (s, 1H), 7.16 (s, 2H), 7.05 (s, 2H), 2.46 (s, 3H), 2.39 (s, 6H) ppm. \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta 149.9\), 143.9, 140.9, 139.3, 138.6, 129.8, 127.9, 125.1, 120.1, 118.8 (d, \(J = 320.7\) Hz), 117.0, 21.5, 21.4 ppm. \(^{1}\)RMS: calcd for C\(_{16}\)H\(_{16}\)F\(_3\)N\(_2\)O\(_3\)S, 362.1038 (M\(^++\)); found, 362.1032.

Procedure to prepare 3',5,5'-trimethyl-N-phenyl-[1,1'-biphenyl]-3-amine (4c).\(^6\)

A flame-dried vial was charged with Pd(OAc)\(_2\) (1.1 mg, 0.005 mmol), BINAP (5.0 mg, 0.008 mmol), Cs\(_2\)CO\(_3\) (45.6 mg, 1.4 equiv) and 4f (34.4 mg, 0.1 mmol) in PhMe (0.1 M). Aniline (11 µL, 0.12 mmol) was added at room temperature under an argon atmosphere. The reaction mixture was allowed to stir at 120 °C for 16 h. The mixture was then filtered through a small plug of silica with EtOAc (4 × 5 mL), the filtrate was evaporated to dryness, the crude product was purified by column chromatography (hexanes:EtOAc 85:15) to afford 3',5,5'-trimethyl-N-phenyl-[1,1'-biphenyl]-3-amine (4c) as a brown oil (27.6 mg, 96%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.30\)–7.26 (m, 2H), 7.18 (s, 2H), 7.12–7.10 (m, 3H), 6.99–6.98 (m, 2H), 6.96–6.92 (m, 1H), 6.88 (s, 1H), 5.72 (s, 1H), 2.37 (s, 9H) ppm. \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta 143.4\), 143.3, 142.7, 141.3, 139.5, 138.2, 129.4, 128.9, 125.1, 121.1, 120.9, 117.9, 117.4, 114.0, 21.6, 21.4 ppm. \(^{1}\)RMS: calcd for C\(_{21}\)H\(_{22}\)N, 288.1674 (M+H\(^+\)); found, 288.1747.
A solution of Na$_2$CO$_3$ (21.2 mg, 0.2 mmol) in degased H$_2$O (1.0 mL) was added to a mixture of Pd(PPh$_3$)$_4$ (0.6 mg, 0.0005 mmol), 4f (34.4 mg, 0.1 mmol) and phenylboronic acid (13.7 mg, 0.112 mmol) in degased monolyme (1.0 mL), under an argon atmosphere. The reaction mixture was stirred at 95 °C for 2.5 h. The mixture was then filtered through a small plug of silica with EtOAc (4 × 5 mL), the filtrate was evaporated to dryness, the crude product was purified by column chromatography (hexanes) to afford 3,5,5′-trimethyl-1,1′:3′,1″-terphenyl (4d) as a colourless oil (26.3 mg, 97%). IR: 3030, 2917, 1560, 1459, 1032, 844, 761, 697 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.65-7.63 (m, 2H), 7.59 (s, 1H), 7.47-7.43 (m, 2H), 7.38-7.33 (m, 3H), 7.26-7.25 (m, 2H), 7.01 (s, 1H), 2.48 (s, 3H), 2.39 (s, 6H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 142.1, 141.7, 141.5, 141.4, 138.7, 138.3, 129.0, 128.8, 127.3, 127.3, 127.0, 126.9, 125.2, 123.5, 21.6, 21.5 ppm. HRMS: calcd for C$_{21}$H$_{21}$, 273.1565 (M+H$^+$); found, 273.1638.

Procedure to prepare 3′,5,5′-trimethyl-[1,1′-biphenyl]-3-yl 4-methylbenzenesulfonate (4g).

Et$_3$N (31 µL, 0.22 mmol) was slowly added to a solution of 3ai (42.4 mg, 0.2 mmol) and p-toluenesulfonyl chloride (41.9 mg, 0.22 mmol) in MeCN (1 mL). The reaction mixture was allowed to stir at room temperature for 1 h. The mixture was then filtered through a small plug of silica with EtOAc (4 × 5 mL), the filtrate was evaporated to dryness, and the crude product was purified by column chromatography (hexanes) to afford 3′,5,5′-trimethyl-[1,1′-biphenyl]-3-yl 4-methylbenzenesulfonate (4g) as a colourless oil (69.5 mg, 95%). IR: 1598, 1358, 1189, 1178, 965, 862, 847, 790, 671 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.76 (d, $J = 8.3$ Hz, 2H), 7.34 (d, $J = 8.0$ Hz, 2H), 7.25 (s, 1H), 7.00 (s, 2H), 6.98 (s, 1H), 6.87 (s, 1H), 6.84 (s, 1H), 2.47 (s, 3H), 2.35 (s, 9H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 149.9, 145.2, 142.8, 140.0, 139.8, 138.3, 132.7, 129.7, 129.4, 128.7, 126.6, 125.0, 121.6, 118.0, 21.7, 21.40, 21.35 ppm. HRMS: calcd for C$_{22}$H$_{36}$NO$_3$S, 384.1628 (M+NH$_4^+$); found, 384.1628.
Procedure to prepare 3',5,5'-trimethyl-[1,1'-biphenyl]-3-carbonitrile (4e).\(^8\)

\[
\text{Et}_3\text{N} (0.1 \mu \text{L}) \text{ was added to a mixture of Pd(OAc)}_2 (0.45 \text{ mg, 0.002 mmol}) \text{ and CM-Phos (3.2 mg, 0.008 mmol) in degased anhydrous DCM (0.5 mL), under an argon atmosphere. The resulting mixture was very gently heated with a heat gun with constant stirring for 5 min. The solvent was then removed under vacuum. 4g (34.4 mg, 0.1 mmol), K}_2\text{CO}_3 (1.7 mg, 0.0125 mmol) \text{ and K}_3[\text{Fe(CN)}_6]\cdot\text{H}_2\text{O (21.1 mg, 0.05 mmol) were charged successively to the tube, and degased }^{1}\text{BuOH (0.25 mL) and H}_2\text{O (0.25 mL) were added as solvent. The reaction mixture was allowed to stir at 80 °C for 18 h. The mixture was then filtered through a small plug of silica with EtOAc (4 × 5 mL), the filtrate was evaporated to dryness, the crude product was purified by column chromatography (hexanes:EtOAc 85:15) to afford 3',5,5'-trimethyl-[1,1'-biphenyl]-3-carbonitrile (4e) as an offwhite solid (21.0 mg, 95%). m. p. 68-70 °C.} \\
\text{IR: 2919, 2227, 1598, 1376, 840, 685 cm}^{-1}. \text{^1H NMR (400 MHz, CDCl}_3) \delta 7.58 (s, 1H), 7.52 (s, 1H), 7.34 (s, 1H), 7.07 (s, 2H), 6.97 (s, 1H), 2.38 (s, 3H), ppm. ^{13}\text{C NMR (101 MHz, CDCl}_3) \delta 142.6, 139.5, 139.1, 134.8, 132.4, 130.9, 129.9, 128.0, 125.0, 119.1, 112.6, 21.4, 21.3 ppm. HRMS: calcd for C}_{16}\text{H}_{16}\text{N, 222.1204 (M+H)}^+; \text{found, 222.1277.}
Silver free arylation of salicylic acids

3',5'-Dimethyl-[1,1'-biphenyl]-3-ol

A mixture of Pd(OAc)$_2$ (5.6 mg, 0.025 mmol), salicylic acid (69.1 mg, 0.50 mmol), Me$_4$NCl (68.5 mg, 0.63 mmol), KOAc (98.0 mg, 1.0 mmol), 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) and acetic acid (43 µL, 0.75 mmol) was heated at 120 °C for 24 h. The mixture was cooled down to room temperature, then extra Me$_4$NCl (44.0 mg, 0.4 mmol) and KOAc (39.0 mg, 0.4 mmol) were added into the mixture and heated at 120 °C for extra 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 3',5'-dimethyl-[1,1'-biphenyl]-3-ol (3aa) as a light orange oil (59.5 mg, 60%). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.29 (t, $J$ = 7.9 Hz, 1H), 7.20 (s, 2H), 7.17-7.15 (m, 1H), 7.07-7.05 (m, 1H), 7.01 (s, 1H), 6.80 (ddd, $J$ = 8.0, 2.6, 0.9 Hz, 1H), 4.76 (s, 1H), 2.38 (s, 6H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 155.7, 143.3, 140.8, 138.3, 129.9, 129.1, 125.1, 119.9, 114.1, 114.0, 21.4 ppm. These data are consistent with those previously reported.²

3',4,5'-Trimethyl-[1,1'-biphenyl]-3-ol

A mixture of Pd(OAc)$_2$ (5.6 mg, 0.025 mmol), 2-hydroxy-3-methylbenzoic acid (76.1 mg, 0.50 mmol), Me$_4$NCl (68.5 mg, 0.63 mmol), KOAc (98.0 mg, 1.0 mmol), 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) and acetic acid (43 µL, 0.75 mmol) was heated at 120 °C for 24 h. The mixture was cooled down to room temperature, then extra Me$_4$NCl (44.0 mg, 0.4 mmol) and KOAc (39.0 mg, 0.4 mmol) were added into the mixture and heated at 120 °C for extra 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 3',4,5'-trimethyl-[1,1'-biphenyl]-3-ol (3ac) as an orange oil (59.0 mg, 56%). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.18-7.16 (m, 3H), 7.08 (dd, $J$ = 7.7, 1.7 Hz, 1H), 7.01-7.00 (m, 1H), 6.98 (s, 1H), 4.69 (s, 1H), 2.37 (s, 6H), 2.29 (s, 3 H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 153.9, 140.8, 140.8, 138.2, 131.2, 128.8, 124.9, 122.5, 119.6, 113.7, 21.4, 15.4 ppm. These data are consistent with those previously reported.²
A mixture of Pd(OAc)$_2$ (5.6 mg, 0.025 mmol), 2-hydroxy-4-methylbenzoic acid (76.1 mg, 0.50 mmol), Me$_4$NCl (68.5 mg, 0.63 mmol), KOAc (98.0 mg, 1.0 mmol), 1-iodo-3,5-dimethylbenzene (218 µL, 1.5 mmol) and acetic acid (43 µL, 0.75 mmol) was heated at 120 ºC for 24 h. The mixture was cooled down to room temperature, then extra Me$_4$NCl (44.0 mg, 0.4 mmol) and KOAc (39.0 mg, 0.4 mmol) were added into the mixture and heated at 120 ºC for extra 16 h. After this time, the reaction mixture was filtered through a plug of Celite® with EtOAc (4 × 5 mL). The filtrate was evaporated to dryness. The crude product was purified by column chromatography (hexanes:EtOAc 90:10) to afford 3',5,5'-trimethyl-[1,1'-biphenyl]-3-ol (3ai) as a light orange solid (74.1 mg, 70%). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.18 (s, 2H), 6.99-6.97 (m, 2H), 6.85-6.84 (m, 1H), 6.63 (s, 1H), 4.66 (s, 1H), 2.37 (s, 6H), 2.36 (s, 3H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 155.7, 143.1, 140.9, 139.9, 138.2, 129.0, 125.0, 120.8, 114.8, 111.3, 21.44, 21.37 ppm. These data are consistent with those previously reported.$^2$
References

Spectroscopic data