Tertiary-Amino-Functionalized Resin-Supported Palladium Catalyst for the Heterogeneous Suzuki–Miyaura Reaction of Aryl Chlorides

Yasunari Monguchi,* Tomohiro Ichikawa, Moeko Netsu, Tomohiro Hattori, Tomoteru Mizusaki, Yoshinari Sawama, and Hironao Sajiki*

a Laboratory of Organic Chemistry, Gifu Pharmaceutical University, 1-25-4 Daigaku-nishi, Gifu 501-1196, Japan
b Chemical Catalysts R&D Department, Catalyst Development Center, N.E. Chemcat Corporation, 25-3 Kojindaira, Bando, Ibaraki 306-0608, Japan

Supporting Information
General
The \(^1\)H NMR and \(^1\)H NMR spectra were recorded on a JEOL JNM ECA-500 (500 MHz for \(^1\)H NMR and 125 MHz for \(^1\)H NMR), ECS-400 (400 MHz for \(^1\)H NMR and 100 MHz for \(^1\)H NMR), or AL-400 (400 MHz for \(^1\)H NMR and 100 MHz for \(^1\)H NMR) spectrometer. CDCl\(_3\) was used as the solvent for NMR measurement. Chemical shifts (\(\delta\)) are expressed in part per million and internally referenced (0.00 ppm for tetramethylsilane for \(^1\)H NMR and 77.0 ppm for CDCl\(_3\)). Mass spectra (EI) were taken on a JEOL JMS Q1000GC Mk II Quad GC/MS. The Hitachi HD-2000 STEM, ULVAC-PHI PHI QuanteraSX M, and Shimadzu ICPS-8100 were used for the scanning transmission electron microscope (STEM) analysis, X-ray photoelectron spectroscopy (XPS), and inductively coupled plasma-atomic emission spectroscopy (ICP-AES), respectively. All products are known compounds, and their \(^1\)H and \(^1\)H NMR spectra were identical with those in the literature.

Preparation of 7\% Pd/WA30 (Scheme 1)
A mixture of the lyophilized DIAION WA30 [3.00 g (net)] in a solution of Pd(OAc)\(_2\) [476 mg, 2.12 mmol (226 mg, palladium quantity)] in EtOAc (30 mL) was stirred under an Ar atmosphere at rt for 4 days. The resulting reddish solid was collected on a Kiriyama funnel (1 \(\mu\)m), washed with EtOAc (20 mL \(\times\) 5), H\(_2\)O (20 mL \(\times\) 5), and MeOH (20 mL \(\times\) 5), and dried under vacuum for 12 h. The filtrate was concentrated in vacuo and then transferred to a 100 mL volumetric flask with H\(_2\)O. Its atomic absorption analysis indicated that 1.78 ppm (178 \(\mu\)g) of palladium species was present. The collected solid was then stirred with NH\(_2\)NH\(_2\)·H\(_2\)O (319 mg, 6.37 mmol) in H\(_2\)O (30 mL) under Ar at rt for 1 d. The black solid was collected on a Kiriyama funnel (1 \(\mu\)m), washed with H\(_2\)O (20 mL \(\times\) 5) and MeOH (20 mL \(\times\) 5), then dried under vacuum for 12 h to produce the Pd/WA30 (3.43 g). The filtrate was concentrated in vacuo and then transferred to a 100 mL volumetric flask with H\(_2\)O. Its atomic absorption analysis indicated that 0.12 ppm (12 \(\mu\)g) of the palladium species was present. The palladium amount, which was not captured on WA30, was found to be 190 \(\mu\)g (178 + 12 \(\mu\)g), which means that the palladium ratio of Pd/WA30 was 6.6% \(((226-0.19)/3430 \times 100\)).

Typical procedure for the 7\% Pd/WA30-catalyzed Suzuki–Miyaura reaction between aryl chlorides and arylboronic acids (Table 2 and Scheme 2)
In the test tube were placed 7\% Pd/WA30 (19.0 mg, 12.5 \(\mu\)mol), the aryl chloride (250 \(\mu\)mol), the arylboronic acid (375 \(\mu\)mol), Cs\(_2\)CO\(_3\) (163 mg, 500 \(\mu\)mol) and DMA (1 mL). The mixture was stirred at 80 °C under an Ar atmosphere. The reaction progress was monitored by TLC analysis (hexane/EtOAc, 5:1). When the reaction was completed within 24 h, the mixture was cooled to rt, diluted with Et\(_2\)O (5 mL), and passed through a cotton filter. The catalyst on the filter was washed with Et\(_2\)O (15 mL \(\times\) 2) and H\(_2\)O (10 mL \(\times\) 3). The combined filtrates were separated into two layers. The aqueous layer was extracted with Et\(_2\)O (20 mL), and the combined organic layers were washed with H\(_2\)O (20 mL \(\times\) 4) and brine (20 mL), dried over Na\(_2\)SO\(_4\), filtered, and concentrated in vacuo. To the residue was added CDCl\(_3\) (ca. 1 mL) and 1,4-dioxane (8.53 \(\mu\)L, 100 \(\mu\)mol). After the determination of the reaction yield by \(^1\)H NMR, the product was purified by silicagel column chromatography using hexane–EtOAc (10:1) as eluents to give the corresponding biaryl. When the reaction was incomplete after 24 h, the reaction mixture was treated in the same manner as described above.
3.81 mmol-scale reaction between 4'-chloroacetophenone and phenylboronic acid

In the 50-mL round bottom-flask were placed 7% Pd/WA30 (285 mg, 188 μmol), 4'-chloroacetophenone (589 mg, 3.81 mmol), phenylboronic acid (586 mg, 5.63 mmol), Cs₂CO₃ (2.44 g, 7.50 mmol) and DMA (15 mL). The mixture was stirred at 80 °C under an Ar atmosphere. After 12 h, the mixture was cooled to rt, diluted with Et₂O (10 mL), and passed through a cotton filter. The catalyst on the filter was washed with Et₂O (20 mL × 2) and H₂O (20 mL × 2). The combined filtrates were separated into two layers. The aqueous layer was extracted with Et₂O (40 mL), and the combined organic layers were washed with H₂O (20 mL × 4) and brine (20 mL), dried over Na₂SO₄, and filtered. The organic layers were transferred to a 200-mL volumetric flask, and Et₂O was added to 200 mL. The aqueous layers were also transferred to a 200-mL volumetric flask, and water was added to 200 mL. 500 μL was sampled from the volumetric flask for organic layers, and concentrated in vacuo. To the residue was added CDCl₃ (ca. 0.5 mL) and 1,4-dioxane (4.25 μL, 50.0 μmol). The ¹H NMR analysis indicated that the reaction was completed and 4-phenyl-acetophenone was obtained in 93% yield. No palladium was detected from both layers by the ICP-AES. XPS and STEM of recovered 7% Pd/WA30 were measured.

XPS of recovered 7% Pd/WA30 after the reaction

After the reaction, the ratio of amount of Pd(0) to Pd(II) increased.

STEM image of recovered 7% Pd/WA30

The size and distribution of Pd species were virtually the same as those before the reaction.
Reuse test of 9% Pd/WA30

Eight test tubes were prepared, and 7% Pd/WA30 (19.0 mg, 12.5 μmol), the 4'-chloroacetophenone (32.5 μL, 250 μmol), phenylboronic acid (45.7 mg, 375 μmol), Cs₂CO₃ (163 mg, 500 μmol) and DMA (1 mL) were placed in each tube. The mixture in each test tube was stirred at 80 °C under an Ar atmosphere (balloon) for 9 h, then all the mixtures were filtered using a Kiriyama funnel (1 μm filter paper). The catalyst on the filter was washed with Et₂O (10 mL × 4) and H₂O (10 mL × 6). The combined filtrates were separated into two layers. The aqueous layer was extracted with Et₂O (20 mL), and the combined organic layers were washed with H₂O (20 mL × 2) and brine (20 mL), dried over Na₂SO₄, filtered, and concentrated in vacuo. To the residue was added CDCl₃ (ca. 1 mL) and 1,4-dioxane (8.53 μL, 100 μmol), and the yield of 4-acetylbiphenyl was determined to be 100% by ¹H NMR. The catalyst on the filter was washed with Et₂O (15 mL × 2) and H₂O (10 mL × 3). The recovered catalyst was dried at room temperature under reduced pressure for 12 h, then weighed [150 mg, 99%, 150 ÷ (19.0 × 8) × 100]. The reaction for the second run was carried out in the same manner as the first run, but using five test tubes [total 4'-chloroacetophenone amount, 163 μL (32.5 μL × 5), 1.25 mmol (0.250 mmol × 5); total phenylboronic acid amount, 229 mg (45.7 mg × 5), 1.88 mmol (0.375 mmol × 5); total Cs₂CO₃ amount, 815 mg (163 mg × 5), 2.50 mmol (500 μmol × 5); total catalyst amount, 95.0 mg (19.0 mg × 5)]. 4-Acetophenone was obtained in 100% yield after 24 h by ¹H NMR using 1,4-dioxane (8.53 μL, 100 μmol) as an internal standard, and the catalyst was recovered (94.3 mg, 99%). The reactions for the third to fifth runs were also carried out in the same manner as the first run except for the number of used test tubes. The results are summarized in the following table.

<table>
<thead>
<tr>
<th>Run</th>
<th>Numer of test tubes</th>
<th>Reaction Time (h)</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Substrate &amp; Reagents</td>
</tr>
<tr>
<td>1st</td>
<td>8</td>
<td>9</td>
<td>4'-Chloroacetophenone 260 μL (2.00 mmol) [32.5 μL (250 μmol) × 8]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Phenylboronic acid 366 mg (3.00 mmol) [45.7 mg (375 μmol) × 8]</td>
</tr>
<tr>
<td>Series</td>
<td>Time (h)</td>
<td>Yield (%)</td>
<td></td>
</tr>
<tr>
<td>------</td>
<td>---------</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td>2nd 5 24</td>
<td>95.0 mg (62.5 μmol) [19.0 mg (12.5 μmol) × 5]</td>
<td>94.3 mg (99%)</td>
<td>100%</td>
</tr>
<tr>
<td>3rd 3 24</td>
<td>57.0 mg (37.5 μmol) [19.0 mg (12.5 μmol) × 3]</td>
<td>56.1 mg (98%)</td>
<td>76%</td>
</tr>
</tbody>
</table>

[a] The yield was determined by $^1$H NMR analysis using 1,4-dioxane as an internal standard.

**Time-course study of the cross-coupling in the filtrate after removal of 7% Pd/WA30 by hot filtration**

Standard run: Four test tubes were prepared, and the cross-coupling of 4'-chloroacetophenone (38.6 mg, 250 μmol) with phenylboronic acid (45.7 mg, 375 μmol) under Ar atmosphere was carried out using Cs₂CO₃ (163 mg, 500 μmol) and 7% Pd/WA30 (19.0 mg, 12.5 μmol) in DMA (1 mL) at 80 °C in each test tube. The reaction mixture was treated after 1 h, 2 h, 3.5 h, or 6 h, according to the general procedure for the 7% Pd/WA30-catalyzed Suzuki–Miyaura reaction. Et₂O extracts of each reaction mixture were concentrated in vacuo, and yield of 4-acetylbiphenyl was determined by $^1$H NMR using 1,4-dioxane (8.53 μL, 100 μmol) as an internal standard (10%, 71%, 93%, and 100% after 1 h, 2 h, 3.5 h, and 6 h, respectively).

Hot filtration: Three test tubes were prepared, and the cross-coupling of 4'-chloroacetophenone (77.3 mg, 500 μmol) with phenylboronic acid (91.4 mg, 750 μmol) under Ar atmosphere was carried out using Cs₂CO₃ (326 mg, 1.00 mmol) and 7% Pd/WA30 (38.0 mg, 25.0 μmol) in DMA (2 mL) at 80 °C in each test tube. After 1 h, 1 mL of each reaction mixture in the three test tubes was filtered using a 0.45-μm Millipore membrane filter without cooling. Each filtrate was heated again at 80 °C for 1 h, 2.5 h, or 5 h, then H₂O (10 mL) was added. The aqueous layer was extracted with Et₂O (15 mL × 2), and combined organic layers were washed with H₂O (10 mL × 3) and brine (10 mL), dried over Na₂SO₄, filtered, and concentrated in vacuo. The yields of 4-acetylbiphenyl after reheating for 1 h,
2.5 h, and 5 h were determined using the same procedure for the standard run (27%, 34%, and 41%, respectively).

Unreduced 7% Pd/WA30-catalyzed Suzuki–Miyaura reaction between 4'-chloroacetophenone and phenylboronic acid

According to the above-mentioned typical procedure, the reaction was carried out using 7% Pd/WA30, which was prepared without the reduction process by NH₂NH₂·H₂O after immersing DIAION WA30 in a solution of Pd(OAc)₂ in EtOAc. The yield of 4-acetylbiphenyl after 6 h was determined to be 97% by ¹H NMR using 1,4-dioxane (8.53 µL, 100 µmol) as an internal standard, together with recovered 4'-chloroacetophenone in 1% yield.

Swelling test of 7% Pd/WA30 and 10% Pd/HP20 by DMA

7% Pd/WA30 (100 mg) was placed in a micro tube, and DMA (500 µL, 470 mg) was added. The mixture was left at room temperature for 6 h. The 7% Pd/WA30 was filtered using a cotton filter, and weighed (198 mg). The recovered 7% Pd/WA30 was placed in a micro tube and compared with dried (fresh) 7% Pd/WA30 (D vs. C, figure below).

10% Pd/HP20, which was prepared by the immobilization of palladium (0) on synthetic adsorbent, DIAION HP20, was also treated in the same manner as 7% Pd/WA30. The weight of swelled 10% Pd/HP20 was 353 mg.

(A) Fresh 10% Pd/HP20 before welling test; (B) 10% Pd/HP20 after swelling test; (C) fresh 7% Pd/WA30 before welling test; (D) 7% Pd/WA30 after swelling test.
Spectral Data of Products

4-Acetylbiphenyl [CAS Reg. No. 92-91-1] (Table 1, entry 14 and Table 2, entry 1)\(^1\)
Obtained in 100% yield (48.6 mg, 248 \(\mu\)mol) from 4’-chloroacetophenone (38.3 mg, 248 \(\mu\)mol) and phenylboronic acid (45.7 mg, 375 \(\mu\)mol).

\(^1\)H NMR (500 MHz) \(\delta\) 8.04 (2H d, \(J = 8.5\) Hz), 7.69 (2H, d, \(J = 8.5\) Hz), 7.64 (2H, d, \(J = 7.3\) Hz), 7.48 (2H, t, \(J = 7.3\) Hz), 7.41 (1H t, \(J = 7.3\) Hz), 2.65 (3H, s); \(^13\)C NMR (125 MHz) \(\delta\) 197.8, 145.8, 139.8, 135.8, 128.9, 128.9, 128.2, 127.3 127.2, 26.7; MS (EI) \(m/z\) (%) 196 (M\(^+\)), 181 (100).

3-Acetylbiphenyl [CAS Reg. No. 3112-01-4] (Table 2, entry 2)\(^2\)
Obtained in 80% yield (38.9 mg (198 \(\mu\)mol) from 3’-chloroacetophenone (38.3 mg, 248 \(\mu\)mol) and phenylboronic acid (61.0 mg, 500 \(\mu\)mol).

\(^1\)H NMR [400 MHz (AL-400)] \(\delta\) 8.18 (1H, s), 7.93 (1H, d, \(J = 7.4\) Hz), 7.79 (1H, d, \(J = 7.4\) Hz), 7.62 (2H, d, \(J = 7.3\) Hz), 7.53 (1H, t, \(J = 7.4\) Hz), 7.47 (2H, t, \(J = 7.3\) Hz), 7.38 (1H, t, \(J = 7.3\) Hz), 2.65 (3H, s) ; \(^13\)C NMR [100 MHz (AL-400)] \(\delta\) 198.1, 141.7, 140.1, 137.6, 131.7, 129.0, 128.9, 127.8 127.2, 126.9 (2C), 26.7; MS (EI) \(m/z\) (%) 196 (M\(^+\)), 181 (100).

2-Acetylbiphenyl [CAS Reg. No. 2142-66-7] (Table 2, entry 3)\(^2\)
Obtained in 89% yield (43.6 mg, 222 \(\mu\)mol) from 2’-chloroacetophenone (38.4 mg, 249 \(\mu\)mol) and phenylboronic acid (61.0 mg, 500 \(\mu\)mol).

\(^1\)H NMR [400 MHz (AL-400)] \(\delta\) 7.49–7.56 (2H, m), 7.33–7.45 (7H, m), 2.00 (3H, s); \(^13\)C NMR [100 MHz (AL-400)] \(\delta\) 204.9, 140.8, 140.7, 140.4, 130.7, 130.1, 128.8, 128.6, 127.8, 127.8, 127.4, 126.9 (2C), 60.9, 14.3; MS (EI) \(m/z\) (%) 196 (M\(^+\)), 181 (100).

Ethyl Biphenyl-4-carboxylate [CAS Reg. No. 6301-56-0] (Table 2, entry 4)\(^1\)
Obtained in 94% yield (53.4 mg, 236 \(\mu\)mol) from ethyl 4-chlorobenzoate (46.2 mg, 251 \(\mu\)mol) and phenylboronic acid (45.7 mg, 375 \(\mu\)mol).

\(^1\)H NMR [400 MHz (ECS-400)] \(\delta\) 8.11 (2H, d, \(J = 8.4\) Hz), 7.64 (2H, d, \(J = 8.4\) Hz), 7.61 (2H, d, \(J = 7.4\) Hz), 7.45 (2H, t, \(J = 7.4\) Hz), 7.38(1H, t, \(J = 7.4\) Hz), 4.39 (2H, q, \(J = 7.4\) Hz), 1.40 (3H, t, \(J = 7.4\) Hz); \(^13\)C NMR [100 MHz (ECS-400)] \(\delta\) 166.5, 145.5, 140.0, 130.1, 129.2, 128.9, 128.0, 127.2, 126.9, 60.9, 14.3; MS (EI) \(m/z\) (%) 226 (M\(^+\)), 27, 198 (20) 181 (100).

4-Nitrobiphenyl [CAS Reg. No. 92-93-3] (Table 2, entry 5)\(^1\)
Obtained in 97% yield (48.1 mg, 242 \(\mu\)mol) from 4-chloronitrobenzene (39.4 mg, 250 \(\mu\)mol) and phenylboronic acid (45.7 mg, 375 \(\mu\)mol).

\(^1\)H NMR [400 MHz (ECS-400)] \(\delta\) 8.28 (2H, d, \(J = 8.9\) Hz), 7.72 (2H, d, \(J = 8.9\) Hz), 7.62 (2H, d, \(J = 7.2\) Hz), 7.42–7.51 (3H, m); \(^13\)C NMR [100 MHz (ECS-400)] \(\delta\) 147.6, 147.0, 138.7, 129.1, 128.9, 127.7, 127.3, 124.0; MS (EI) \(m/z\) (%) 199 (M\(^+\)), 152 (100).

4-(Trifluoromethyl)biphenyl [CAS Reg. No. 398-36-7] (Table 2, entry 6)\(^3\)
Obtained in 96% yield (57.0 mg, 257 \(\mu\)mol) from 4-chlorobenzotrifluoride (48.0 mg, 266 \(\mu\)mol) and phenylboronic acid (45.7 mg, 375 \(\mu\)mol).

\(^1\)H NMR [400 MHz (ECS-400)] \(\delta\) 7.67 (4H, s), 7.59 (2H, d, \(J = 7.4\) Hz), 7.46 (2H, t, \(J = 7.4\) Hz), 7.39 (1H, t, \(J = 7.4\) Hz); \(^13\)C NMR [100 MHz (ECS-400)] \(\delta\) 144.7, 139.8, 129.3 (\(J_{C-F} = 32\) Hz), 129.0, 128.2, 127.4, 127.3, 125.7
4-Methoxybiphenyl [CAS Reg. No. 613-37-6] (Table 2, entry 7)
Obtained in 64% yield (29.7 mg, 161 µmol) from 4-chloroanisole (35.7 mg, 251 µmol) and phenylboronic acid (91.4 mg, 750 µmol) using 7%Pd/WA30 (38.0 mg, 25.0 µmol) and Cs₂CO₃ (244.4 mg, 750 µmol).

1H NMR [400 MHz (AL-400)] δ 7.55 (2H, d, J = 7.7 Hz), 7.52 (2H, d, J = 8.8 Hz), 7.41 (2H, t, J = 7.7 Hz), 7.30 (1H, t, J = 7.7 Hz), 6.97 (2H, d, J = 8.8 Hz), 3.84 (3H, s); 13C NMR [100 MHz (AL-400)] δ 159.1, 140.8, 133.7, 128.7, 128.1, 126.7, 126.6, 114.2, 55.3; MS (EI) m/z (%) 184 (M⁺, 100).

3-Methoxybiphenyl [CAS Reg. No. 2113-56-6] (Table 2, entry 8)
Obtained in 83% yield (37.9 mg, 206 µmol) from 3-chloroanisole (35.5 mg, 249 µmol) and phenylboronic acid (91.4 mg, 750 µmol) using 7%Pd/WA30 (38.0 mg, 25.0 µmol) and Cs₂CO₃ (244.4 mg, 750 µmol).

1H NMR [400 MHz (ECS-400)] δ 7.58 (2H, d, J = 7.1 Hz), 7.42 (2H, t, J = 7.1 Hz), 7.32–7.36 (2H, m), 7.17 (1H, d, J = 8.2 Hz), 7.12 (1H, s), 6.89 (1H, d, J = 8.2 Hz), 3.85 (3H, s); 13C NMR [100 MHz (ECS-400)] δ 159.9, 142.8, 141.1, 129.7, 128.7, 127.4, 127.2, 119.7, 112.9, 112.7, 55.3; MS (EI) m/z (%) 184 (M⁺, 100).

2-Methoxybiphenyl [CAS Reg. No. 86-26-0] (Table 2, entry 9)
Obtained in 15% yield (6.9 mg, 38 µmol) from 2-chloroanisole (35.6 mg, 250 µmol) and phenylboronic acid (91.4 mg, 750 µmol) using 7%Pd/WA30 (38.0 mg, 25.0 µmol) and Cs₂CO₃ (244.4 mg, 750 µmol).

1H NMR (500 MHz) δ 7.54 (2H, d, J = 7.7 Hz), 7.42 (2H, t, J = 7.7 Hz), 7.31–7.35 (3H, m), 7.04 (1H, t, J = 8.0 Hz), 7.00 (1H, d, J = 8.0 Hz) 3.82 (3H, s); 13C NMR (125 MHz) δ 156.4, 138.5, 130.9, 130.6, 129.5, 128.6, 128.0, 126.9, 120.8, 111.1, 55.5; MS (EI) m/z (%) 184 (M⁺, 100).

4-Acetyl-4'-methoxybiphenyl [CAS Reg. No. 13021-18-6] (Table 2, entry 10)
Obtained in 96% yield (54.2 mg, 240 µmol) from 4'-chloroacetophenone (38.5 mg, 249 µmol) and 4-methoxyphenylboronic acid (57.0 mg, 375 µmol).

1H NMR [400 MHz (AL-400)] δ 8.00 (2H, d, J = 8.8 Hz), 7.64 (2H, d, J = 8.8 Hz), 7.57 (2H, d, J = 8.8 Hz), 6.99 (2H, d, J = 8.8 Hz), 7.00 (1H, d, J = 8.0 Hz) 4.41 (2H, q, J = 7.1 Hz), 2.64 (3H, s), 1.42 (3H, t, J = 7.1 Hz); 13C NMR [100 MHz (ECS-400)] δ 197.7, 159.9, 145.3, 135.2, 132.1, 128.9, 128.3, 126.6, 114.4, 55.3, 26.6; MS (EI) m/z (%) 226 (M⁺, 59), 211 (100).

Ethyl 4'-Acetyl-4-biphenylcarboxylate [CAS Reg. No. 119838-61-8] (Table 2, entry 11)
Obtained in 91% yield (60.9 mg, 227 µmol) from ethyl 4-chlorobenzoate (46.1 mg, 250 µmol) and 4-acetylphenylboronic acid (91.4 mg, 750 µmol) using 7%Pd/WA30 (38.0 mg, 25.0 µmol) and Cs₂CO₃ (244.4 mg, 750 µmol).

1H NMR [400 MHz (AL-400)] δ 8.13 (2H, d, J = 9.0 Hz), 8.04 (2H, d, J = 8.8 Hz), 7.64 (2H, d, J = 8.8 Hz), 7.57 (2H, d, J = 8.8 Hz), 6.99 (2H, d, J = 8.8 Hz), 7.00 (1H, d, J = 8.0 Hz) 4.41 (2H, q, J = 7.1 Hz), 2.64 (3H, s), 1.42 (3H, t, J = 7.1 Hz); 13C NMR [100 MHz (ECS-400)] δ 197.7, 166.2, 144.4, 144.0, 136.3, 130.1, 128.9, 127.3, 127.1, 61.0, 26.6, 14.3; MS (EI) m/z (%) 268 (M⁺, 32), 253 (100).

4-Methoxy-4'-methylbiphenyl [CAS Reg. No. 53040-92-9] (Table 2, entry 12)
Obtained in 78% (38.4 mg, 194 µmol) from 4-chlorotoluene (31.6 mg, 250 µmol) and phenylboronic acid (91.4 mg, 750 µmol) using 7%Pd/WA30 (38.0 mg, 25.0 µmol) and Cs₂CO₃ (244.4 mg, 750 µmol).

1H NMR (500 MHz) δ 7.51 (2H, d, J = 8.6 Hz), 7.45 (2H, d, J = 8.3 Hz), 7.22 (2H, d, J = 8.3 Hz), 6.96 (2H, d, J = 8.6 Hz), 3.84 (3H, s), 2.38 (3H, s); 13C NMR (125 MHz) δ 158.9, 137.9, 136.3, 133.7, 129.4, 127.9, 126.6, 114.1, 55.3, 21.0; MS (EI) m/z (%) 198 (M⁺, 100).
4-Methoxy-3'-methylbiphenyl [CAS Reg. No. 17171-17-4] (Table 2, entry 13)\(^7\)

Obtained in 79% (39.0 mg, 197 \(\mu\)mol) from 3-chlorotoluene (31.6 mg, 250 \(\mu\)mol) and 4-methoxyphenylboronic acid (57.0 mg, 375 \(\mu\)mol).

\(^1\)H NMR (500 MHz) \(\delta\) 7.51 (2H, d, \(J = 8.5\) Hz), 7.36 (1H, s, \(J = 7.5\) Hz), 7.35 (1H, d, \(J = 7.5\) Hz), 7.30 (1H, t, \(J = 7.5\) Hz), 6.96 (2H, d, \(J = 8.5\) Hz), 3.83 (3H, s); 13C NMR (125 MHz) \(\delta\) 159.0, 140.8, 138.2, 133.8, 128.6, 128.1, 127.5, 127.4, 123.8, 114.1, 55.3, 21.5; MS (EI) \(m/z\) (%) 198 (M\(^+\), 100).

4-Methoxy-2'-methylbiphenyl [CAS Reg. No. 92495-54-0] (Table 2, entry 14)\(^7\)

Obtained in 66% yield (32.7 mg, 165 \(\mu\)mol) from 2-chlorotoluene (31.6 mg, 250 \(\mu\)mol) and 4-methoxyphenylboronic acid (57.0 mg, 375 \(\mu\)mol).

\(^1\)H NMR (500 MHz) \(\delta\) 7.21–7.27 (6H, m), 6.95 (2H, d, \(J = 9.0\) Hz), 3.84 (3H, s), 2.28 (3H, s); 13C NMR (125 MHz) \(\delta\) 158.4, 141.5, 135.4, 134.3, 130.3, 130.2, 129.9, 126.9, 125.7, 113.4, 55.2, 20.5; MS (EI) \(m/z\) (%) 198 (M\(^+\), 100).

4-Acetyl-4'-methylbiphenyl [CAS Reg. No. 5748-38-9] (Table 2, entry 15)\(^6\)

Obtained in 71% yield (37.1 mg, 176 \(\mu\)mol) from 4-chlorotoluene (31.6 mg, 250 \(\mu\)mol) and 4-acetylphenylboronic acid (82.0 mg, 500 \(\mu\)mol).

\(^1\)H NMR [400 MHz (ECS-400)] \(\delta\) 8.05 (2H, d, \(J = 8.4\) Hz), 7.65 (2H, d, \(J = 8.4\) Hz), 7.52 (2H, d, \(J = 7.8\) Hz), 7.27 (2H, d, \(J = 7.8\) Hz), 2.61 (3H, s), 2.40 (3H, s); 13C NMR [100 MHz (ECS-400)] \(\delta\) 197.7, 145.7, 138.2, 136.9, 135.6, 129.6, 128.9, 127.0, 126.9, 26.6, 21.1; MS (EI) \(m/z\) (%) 210 (M\(^+\), 82), 195 (100).

4-Phenylpyridine [CAS Reg. No. 939-23-1] (Scheme 2)\(^8\)

Obtained in 100% yield (38.7 mg, 249 \(\mu\)mol) from 4-chloropyridine hydrochloride (37.5 mg, 250 \(\mu\)mol) and phenylboronic acid (45.7 mg, 375 \(\mu\)mol) using Cs\(_2\)CO\(_3\) (244.4 mg, 750 \(\mu\)mol).

\(^1\)H NMR (500 MHz) \(\delta\) 8.66 (2H, d, \(J = 6.0\) Hz), 7.64 (2H, d, \(J = 7.0\) Hz), 7.43–7.51 (5H, m); 13C NMR (125 MHz) \(\delta\) 150.2, 148.3, 138.1, 129.1, 129.0, 127.0, 126.9, 121.6; MS (EI) \(m/z\) (%) 155 (M\(^+\), 100).

References

4-Acetylbiphenyl (Table 1, entry 14 and Table 2, entry 1)

**1H NMR Spectrogram:**

![1H NMR Spectrum of 4-Acetylbiphenyl](ICH-3-87_CDCl3_ECA500_1H)

**13C NMR Spectrogram:**

![13C NMR Spectrum of 4-Acetylbiphenyl](ICH-3-87_CDCl3_ECA500_13C)
3-Acetyl biphenyl (Table 2, entry 2)
2-Acetylbiphenyl (Table 2, entry 3)
**Ethyl Biphenyl-4-carboxylate (Table 2, entry 4)**

- **Proton NMR (1H):**
  - Parts per Million: 8.0, 7.0, 6.0, 5.0, 4.0, 3.0, 2.0, 1.0, 0.0
  - Peaks at 4.05, 3.00, 2.04, 1.98, 0.99

- **Carbon-13 NMR (13C):**
  - Parts per Million: 200.0, 190.0, 180.0, 170.0, 160.0, 150.0, 140.0, 130.0, 120.0, 110.0, 100.0, 90.0, 80.0, 70.0, 60.0, 50.0, 40.0, 30.0, 20.0, 10.0, 0.0, -10.0
  - Peaks at 140.0, 130.0, 120.0, 110.0, 100.0, 90.0, 80.0, 70.0, 60.0, 50.0, 40.0, 30.0, 20.0, 10.0, 0.0, -10.0
4-Nitrobiphenyl (Table 2, entry 5)

ICH-3-90-b-010-21-CDECS-ECS400

\[
\ce{\text{NO}_2}
\]

ICH-3-90-b-010-21-CDECS-ECS400_13C

\[
\ce{\text{NO}_2}
\]
4-(Trifluoromethyl)biphenyl (Table 2, entry 6)
4-Methoxybiphenyl (Table 2, entry 7)

ICH-3-05_E2S-31 CDCl3-400 MHz

ICH-3-05_E2S-31 CDCl3-13C
3-Methoxybiphenyl (Table 2, entry 8)

ICH3-102_f20-27_CDCl3-ECS400_1H

ICH3-102_f20-27_CDCl3-ECS400_13C
4-Acetyl-4’-methoxybiphenyl (Table 2, entry 10)

ICH-3-115_fr32-46_CDCl3_A400_1H

ICH-3-115_fr32-46_CDCl_A400_13C
Ethyl 4'-acetyl-4-biphenylcarboxylate (Table 2, entry 11)
4-Methoxy-4’-methylbiphenyl (Table 2, entry 12)

ICH-3-157_CDCl3_ECA500_1H

ICH-3-157_CDCl3_ECA500_13C
4-Methoxy-3’-methylbiphenyl (Table 2, entry 13)

ICH-3-180_CDCl3_ECA500_1H

ICH-3-180_CDCl3_ECA500_13C
4-Methoxy-2'-methylbiphenyl (Table 2, entry 14)

ICH-3-181_CDCl3_ECA500_1H

ICH-3-181_CDCl3_ECA500_13C
4-Acetyl-4’-methylbiphenyl (Table 2, entry 15)
4-Phenylpyridine (Scheme 2)