Supporting Information

Palladium and copper-catalyzed ligand-free coupling of phenylhydrazines in water

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General Experimental Details:

All glass apparatus were oven dried prior to use. Melting points were determined in open capillary tubes on an electrically heated block and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR RX1 spectrophotometer. $^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker DRX-300 and Bruker Ascend-400 using CDCl$_3$ as solvent and tetramethylsilane as internal reference. Direct Analysis in Real Time Mass spectrometry (DARTMS) was obtained on JMS-T100LC, AccuTOF. Column chromatography was performed over silica gel (60-120 Mesh) by using Smart flash EPCLC AI-700X YAMAZEN with minimal amount of solvent. HPLC analyses was carried out using system consists of Shimazdu LC-10ATVp pumps and SIL-HTc auto sampler with temperature controller on a Zorbax SB100 C18 column ($4.6 \times 150$ mm, 5.0 μm). The system was run in gradient mode with mobile phase consisting of acetonitrile (A) and water (B) at a flow rate of 0.80 mL/min. Data acquisition was carried out on Class Vp software. All chemicals and reagents were obtained from Aldrich (USA), Alfa Aesar (England) and used without further purification. All reactions were performed in a 25 ml RB flask equipped with a guard tube and reaction mixture was stirred at 600 rpm at rt for the duration of reaction.

Representative procedure for the synthesis of 4,4′-difluorobiphenyl (2a):

To a solution of phenylhydrazine 1a (100 mg, 0.62 mmol) in water (10 mL) added Pd(TFA)$_2$ (5.1 mg, 0.015 mmol) and Cu(OAc)$_2$ (11.2 mg, 0.062 mmol) and stirred the reaction mixture at rt for 15 min. The reaction mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na$_2$SO$_4$ and the solvent was removed under reduced pressure to give the crude product. Crude product was further purified by column chromatography over silica gel using 100% hexane as eluent to furnish 53mg (90%) of 2a as white solid.

Representative procedure for the synthesis of 4-fluoro-4′-methoxybiphenyl (3c):

To a solution of phenylhydrazine 1a (110mg, 0.68 mmol) and phenylhydrazine 1h (100mg, 0.57 mmol) in water (10 mL) added Pd(TFA)$_2$ (4.7 mg, 0.014 mmol) and Cu(OAc)$_2$ (10.3mg, 0.057 mmol) and stirred the reaction mixture at rt for 2 h. The reaction mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na$_2$SO$_4$ and the solvent was removed under reduced pressure to give the crude product. Crude product was further purified by column chromatography over silica gel using 100% hexane as eluent. Quantitative yields of cross coupling products were carried out using system consists of Shimazdu LC-10ATVp pumps and SIL-HTc auto sampler with temperature controller to give 71% of 3c, 13% of 2a and 15% of 2h by using Zorbax SB100 C18 column ($4.6 \times 150$ mm, 5.0 μm) eluted with gradient of H$_2$O:Acetonitrile.

Representative procedure for the synthesis of 4-chloro-4′-methoxybiphenyl (3a):
To a solution of 4-Chlorophenylhydrazine hydrochloride 1c (100mg, 0.56 mmol) and 4-Methoxyphenylboronic acid 6 (100mg, 0.66 mmol) in water (10 mL) added Pd(TFA)$_2$ (3.3 mg, 0.010 mmol) and Cu(OAc)$_2$ (10.8mg, 0.06 mmol) and stirred the reaction mixture at rt for 6 h. The reaction mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na$_2$SO$_4$ and the solvent was removed under reduced pressure to give the crude product. Crude product was further purified by column chromatography over silica gel using 100% hexane as eluent and to furnish 62.3mg (51%) of 3a as white solid, 17mg (28%) of 2c as white solid and 12.5mg (18 %) of 2h as white solid.

**Compound Characterization Data:**

**4,4′-difluorobiphenyl (2a)$^1$**

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\end{array}
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White solid, Yield 90%, mp 78-81°C, lit$^1$ mp 88-90°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3021, 1601, 1497, 928; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.10-7.14 (4H, m), 7.47-7.51 (4H, m); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 115.9 (d, $J$= 21.37 Hz, 4×CH), 128.8 (d, $J$= 8.0 Hz, 4×CH), 136.6 (d, $J$= 2.95 Hz, 2×C), 164.2 (d, $J$= 244.93 Hz, 2xC-F); **HRMS** (DART) m/z calcd for C$_{12}$H$_8$F$_2$ (M)$^+$ 190.0594, found 190.0603.

**4,4′-dibromobiphenyl (2b)$^1$**

\[
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\text{Br}
\end{array}
\]

White solid, Yield 85%, mp 158-162°C, lit$^1$ mp 162-164°C, ; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3021, 1634, 1473, 928; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40-7.43 (4H, m), 7.55-7.58 (4H, m); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 122.1 (2×C), 128.6 (4×CH), 132.2 (4×CH), 139.0 (2×C); **HRMS** (DART) m/z calcd for C$_{12}$H$_8$Br$_2$ (M)$^+$ 309.8992, found 309.9020.

**4,4′-dichlorobiphenyl (2c)$^1$**

\[
\begin{array}{c} \text{Cl} \\
\text{Cl}
\end{array}
\]

White solid, Yield 90%, mp 142-145°C, lit$^1$ mp 148-150°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3021, 1634, 1478, 928; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40-7.42 (4H, m), 7.46-7.49 (4H, m); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 128.3 (4×CH), 129.2 (4×CH), 133.9 (2×C), 138.5 (2×C); **HRMS** (DART) m/z calcd for C$_{12}$H$_8$Cl$_2$ (M)$^+$ 222.0003, found 221.9995.

**Biphenyl (2d)$^1$**
White solid, Yield 82%, mp 65-68°C, lit1 mp 68-70°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3021, 1631, 1521, 927; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.36 (2H, t, $J = 6.9$ Hz), 7.45 (4H, t, $J = 7.5$Hz), 7.61 (4H, d, $J = 8$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$), $\delta$ 127.3 (4×CH), 127.4 (2×CH), 128.9 (4×CH), 141.4 (2×C), HRMS (DART) $m/z$ calcd for C$_{12}$H$_{10}$ (M$^+$) 154.0783, found 154.0786.

**Biphenyl-4,4′-dicarbonitrile (2e)**

Light Yellow solid, Yield 69%, mp 223-225°C, lit1 mp 235-237°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3019, 2231, 1605, 1493, 928; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.69 (4H, d, $J = 8.5$ Hz), 7.78 (4H, d, $J = 8.4$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$), $\delta$ 112.5 (2×C), 118.5 (2×C), 128.1 (4×CH), 133.0 (4×CH), 143.6 (2×C); HRMS (DART) $m/z$ calcd for C$_{14}$H$_9$N$_2$ (M+H$^+$) 205.0766, found 205.0766.

**4,4′-dinitrobiphenyl (2f)**

White solid, Yield 81%, mp 236-240°C, lit2 mp 235°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3019, 1638, 1480, 928; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.79 (4H, d, $J = 8.7$ Hz), 8.36 (4H, d, $J = 8.7$ Hz); $^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$ 124.5 (4×CH), 128.5 (4×CH), 145.1 (2×C), 148.2 (2×C); HRMS (DART) $m/z$ calcd for C$_{12}$H$_9$N$_2$O$_4$ (M+H$^+$) 245.0562, found 245.0564.

**3,3,4,4′-tetrachlorobiphenyl (2g)**

White solid, Yield 79%, mp 165-168°C, lit3 mp 175-177°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3019, 1635, 1545, 928; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.35-7.37 (2H, dd, $J = 8.3$, 2.1 Hz), 7.51-7.53 (2H, m), 7.62 (2H, d, $J = 2.1$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 126.3 (2×CH), 128.9 (2×CH), 131.1 (2×CH), 132.6 (2×C), 133.4 (2×C), 138.9 (2×C); HRMS (DART) $m/z$ calcd for C$_{12}$H$_6$Cl$_4$ (M$^+$) 289.9223, found 289.9207.

**4,4′-dimethoxybiphenyl (2h)**

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1. Usually refers to a literature source.
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White solid, Yield 68%, mp 165-168°C, lit1 mp 172-174°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3021, 1610, 1499, 928; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.85 (6H, s), 6.95-6.97 (4H, m), 7.47-7.49 (4H, m); $^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$ 55.5 (2×CH$_3$), 114.3 (4×CH), 127.9 (4×CH), 133.6 (2×C), 158.8 (2×C), **HRMS** (DART) $m/z$ calcd for C$_{14}$H$_{15}$O$_2$ (M+H)$^+$ 215.1072, found 215.1075.

3,3,4,4′-tetramethylbiphenyl (2i)$^1$

White solid, Yield 80%, mp 68-70°C, lit1 mp 72-74°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3019, 1637, 1495, 928; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.31 (6H, s), 2.34 (6H, s), 7.19 (2H, d, $J = 7.7$ Hz), 7.37 (2H, d), 7.37 (2H, s); $^{13}$C NMR (100 MHz, CDCl$_3$), $\delta$ 19.5 (2×CH$_3$), 20.0 (2×CH$_3$), 124.5 (2×CH), 128.4 (2×CH), 130.1 (2×CH), 135.4 (2×C), 136.9 (2×C), 139.0 (2×C); **HRMS** (DART) $m/z$ calcd for C$_{16}$H$_{19}$ (M+H)$^+$ 211.1480, found 211.1480.

7,7′-dichloro-4,4′-biquinoline (2j)

Brown solid, Yield 45%, mp 168-170°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3020,1605,1492,878; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.23 (2H, d, $J = 3.8$ Hz), 7.34-7.37 (4H, m), 8.21 (2H, t, $J = 2.04$ Hz), 9.04 (2H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 121.9 (2× CH), 125.1 (2×C) , 126.8 (2×CH), 128.4 (2×CH), 128.9 (2×CH), 136.0 (2×C), 143.8 (2×C), 148.8 (2×C), 150.9 (2×CH), **HRMS** (ESI) $m/z$ calcd for C$_{18}$H$_{10}$Cl$_2$N$_2$ (M+H)$^+$ 325.0299, found 325.0299.

4-chloro-4′-methoxybiphenyl (3a)$^4$

White solid, Yield 76%, mp 105-107°C, lit4 mp 115-116.4°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3021, 1611, 1485, 928; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.85 (3H, s), 6.96-6.99 (2H, m), 7.37-7.39 (2H, m), 7.46-7.50 (4H, m); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 55.5 (CH$_3$), 114.5 (2×CH), 128.1 (2×CH), 128.2 (2×CH), 128.9 (2×CH), 132.6 (C), 132.8 (C), 139.4 (C), 159.5 (C); **HRMS** (DART) $m/z$ calcd for C$_{13}$H$_{11}$ClO (M)$^+$ 218.0498, found 218.0512;

4-bromo-4′-methoxybiphenyl (3b)$^5$
White solid, Yield 75%, mp 136-140°C, lit5 143-145°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3021, 1612, 1481, 928; **$^1$H NMR** (400 MHz, CDCl$_3$) $\delta$ 3.85 (3H, s), 6.96-6.98 (2H, m), 7.40-7.42 (2H, m), 7.47-7.54 (4H, m); **$^{13}$C NMR** (100 MHz, CDCl$_3$), $\delta$ 55.5 (CH$_3$), 114.5 (2×CH), 120.9 (C), 128.1 (2×CH), 128.4 (2×CH), 131.9 (2×CH), 132.6 (C), 139.9 (C), 159.6 (C); HRMS (DART) m/z calcd for C$_{13}$H$_{12}$BrO (M+H)$^+$ 263.0072, found 263.0064;

**4-fluoro-4′-methoxybiphenyl (3c)$^6$**

White solid, Yield 71%, mp 90-94°C, lit$^6$ mp 84-86°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3021, 1611, 1500, 928; **$^1$H NMR** (400 MHz, CDCl$_3$) $\delta$ 3.85 (3H, s), 6.95-6.99 (2H, m), 7.07-7.13 (2H, m), 7.45-7.52 (4H, m); **$^{13}$C NMR** (100 MHz, CDCl$_3$), $\delta$ 55.4 (CH$_3$), 114.3 (2×CH), 115.6 (d, $J$ = 21.22 Hz, 2×CH), 128.0 (2×CH), 128.3 (d, $J$ = 7.86 Hz, 2×CH), 132.9 (C), 137.0 (C), 159.1 (C), 163.3 (d, $J$ = 243.84 Hz, C-F); HRMS (DART) m/z calcd for C$_{13}$H$_{12}$FO (M+H)$^+$ 203.0872, found 203.0867.

**4′-methoxybiphenyl-4-carbonitrile (3d)$^4$**

White solid, Yield 41%, mp 97-99°C, lit$^4$ mp 114.115.4°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3019, 2228, 1606, 1495, 928; **$^1$H NMR** (400 MHz, CDCl$_3$) $\delta$ 3.87 (3H, s), 6.99-7.02 (2H, m), 7.52-7.56 (2H, m), 7.62-7.65 (2H, m), 7.68-7.71 (2H, m); **$^{13}$C NMR** (100 MHz, CDCl$_3$), $\delta$ 55.5 (CH$_3$), 110.2 (C), 114.7 (2×CH), 119.2 (C), 127.2 (2×CH), 128.5 (2×CH), 131.6 (C), 132.7 (2×CH), 145.4 (C), 160.3 (C); HRMS (DART) m/z calcd for C$_{14}$H$_{12}$NO (M+H)$^+$ 210.0919, found 210.0918.

**4′-chlorobiphenyl-4-carbonitrile (3e)$^4$**

White solid, Yield 59%, mp 117-120°C, lit$^4$ mp 124-125°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3020, 2230 1637, 1485, 929; **$^1$H NMR** (400 MHz, CDCl$_3$) $\delta$ 7.44-7.47 (2H, m), 7.50-7.54 (2H, m), 7.63-7.66 (2H, m), 7.72-7.74 (2H, m); **$^{13}$C NMR** (100 MHz, CDCl$_3$) $\delta$ 111.4 (C), 118.9 (C), 127.7 (2×CH), 128.6 (2×CH), 129.5 (2×CH), 132.8 (2×CH), 135.1 (C), 137.7 (C), 144.5 (C); HRMS (DART) m/z calcd for C$_{13}$H$_9$ClN (M+H)$^+$ 214.0424, found 214.0427.

**4′-bromobiphenyl-4-carbonitrile (3f)$^7$**

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White solid, Yield 64%, mp 116-118°C, lit7 mp 115-115.5°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3021, 2230, 1610, 1482, 928; **$^1$H NMR** (400 MHz, CDCl$_3$) $\delta$ 7.44-7.47 (2H, m), 7.60-7.67 (4H, m), 7.72-7.74 (2H, m); **$^{13}$C NMR** (100 MHz, CDCl$_3$) $\delta$ 111.5 (C), 118.9 (C), 123.3 (C), 127.7 (2×CH), 128.9 (2×CH), 132.4 (2×CH), 132.8 (2×CH), 138.2 (C), 144.6 (C); **HRMS** (DART) m/z calcd for C$_{13}$H$_9$BrN (M+H)$^+$ 257.9918, found 257.9926.

**2-(4-fluorophenyl)benzo[d]thiazole (5)**

Off yellow solid, Yield 47%, mp 95-98°C, lit8 mp 98-100°C; **FT-IR** (KBr, $\nu_{\text{max}}$/cm$^{-1}$) 3019, 1607, 1485, 839; **$^1$H NMR** (400 MHz, CDCl$_3$) $\delta$ 7.17-7.21 (2H, m), 7.39 (1H, td, $J$ = 8.24, 1.08), 7.50 (1H, td, $J$ = 8.24, 1.2), 7.91 (1H, d, $J$ = 7.96), 8.05-8.12 (3H, m); **$^{13}$C NMR** (100 MHz, CDCl$_3$) $\delta$ 116.3 (d, $J$ = 21.99, 2XCH), 121.6 (CH), 123.2 (CH), 125.3 (CH), 126.4 (CH), 129.6 (d, $J$ = 8.6 Hz, 2XCH), 130.0 (C), 135.1 (C), 154.1 (C), 165.8 (d, $J$ = 251.0 Hz, C-F), 166.8 (C); **HRMS** (ESI) m/z calcd for C$_{13}$H$_8$FNS (M+H)$^+$ 230.0439, found 230.0440.

References:

$^1$H NMR Spectra of (2a) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (2a) (75 MHz, CDCl$_3$)
$^1$H NMR Spectra of (2b) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (2b) (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of (2c) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (2c) (75 MHz, CDCl$_3$)
$^1$H NMR Spectra of (2d) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (2d) (100 MHz, CDCl$_3$)
**1H NMR Spectra of (2e) (400 MHz, CDCl₃)**

**13C NMR Spectra of (2e) (100 MHz, CDCl₃)**
\[1^H\text{ NMR Spectra of (2f) (400 MHz, CDCl}_3)\]

\[1^3C\text{ NMR Spectra of (2f) (75 MHz, CDCl}_3)\]
$^1$H NMR Spectra of (2g) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (2g) (100 MHz, CDCl$_3$)
$^{1}H$ NMR Spectra of (2h) (400 MHz, CDCl$_3$)

$^{13}C$ NMR Spectra of (2h) (75 MHz, CDCl$_3$)
$^1$H NMR Spectra of (2i) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (2i) (100 MHz, CDCl$_3$)
$^{1}H$ NMR Spectra of (2j) (400 MHz, CDCl$_3$)

$^{13}C$ NMR Spectra of (2j) (100 MHz, CDCl$_3$)
Dept 90° NMR Spectra of (2j) (400 MHz, CDCl₃)

Dept 135° NMR Spectra of (2j) (400 MHz, CDCl₃)
$^1$H-$^1$H-COSY of (2j) (400 MHz, CDCl$_3$)
HSQC Spectrum of (2j) (400 MHz, CDCl₃)

HSQC Spectrum of (2j) (400 MHz, CDCl₃)
$^{1}$H NMR Spectra of (3a) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (3a) (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of (3b) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (3b) (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of (3c) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (3c) (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of (3d) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (3d) (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of (3e) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (3e) (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of (3f) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (3f) (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of (5) (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of (5) (100 MHz, CDCl$_3$)