Supporting Information
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Supporting information

Efficient Preparation of 2-Aminomethylbiphenyls via Suzuki-Miyaura Reactions

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Unless otherwise indicated, all starting materials were purchased from commercial sources (Aldrich, Fischer and Frontier Scientific) and used without further purification. The reagents and the solvents were dried and purified before use by usual procedures and kept under argon.[1] Water used was distilled and deionised using a Barnstead NANOpower system (Boston, MA) with four purification columns. All reagents were assembled under an inert atmosphere in a Schlenk tube. 1H- and 13C-NMR spectra were recorded on a Varian 400 spectrometer. 11B-NMR spectra were recorded on the same spectrometer using BF3•Et2O as an external reference. All the 11B NMR experiments were done with quartz NMR tubes (Norell). Chemical shifts (δ) are reported in parts per million (ppm) using residual solvents protons as internal standard. The coupling constants are reported in Hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), br (broad singlet) and m (multiplet). Melting points, Mel-Temp®, are uncorrected. Mass spectra were obtained from the Mass Spectrometry Laboratory of the Faculty of Medicine at the University of Toronto, Toronto, Canada. GC/MS data were recorded on a HP 5890 series II chromatograph and HP 5989A mass spectrometer (Column:HP-5) and reported listing the retention time is in minute. Helium was the carrier gas. The following conditions were used for all GC-MS analyses of biphenyls: Injector temperature: 280 °C, initial temperature: 80 °C, temperature increase rate: 10 °C min-1, final temperature: 300 °C, final time: 30 min. HPLC data were recorded on HP1050 with a C18 column (GraceVydac) and a DAD detector. Retention time is in minute followed by the percentage integration of the total chromatogram. All solvents were degassed and gradients of A (89.9% H2O/ 0.1% TFA) and B (9.9% CH3CN/ 0.1% TFA) → C (99.9% CH3CN/ 0.1% TFA) in 35 min were used.
**General procedure for the Suzuki coupling reactions**

A Schlenk tube containing a stirrer bar and fitted with a rubber cap was flame dried *in vacuo* and backfilled with argon. After cooling, the tube was charged with Pd(PPh₃)₄ (2 mol%), and aryl halide (1 eq.), then was evacuated and backfilled with argon three times. Then, toluene was added by syringe under inert atmosphere. The mixture was then stirred at room temperature for 15 minutes. The phenylboronic acid and NaOH (5N, 1 mL) was then added and the Schlenk tube was evacuated and backfilled with argon three times. The reaction mixture was stirred for the required reaction time (determined by GC/MS analysis) in an oil bath at 100-110°C. The reaction mixture was diluted with ethyl ether, filtered through a pad of celite and then evaporated. The crude material was purified by column chromatography on silica gel (eluting with hexanes/ethyl acetate mixtures).

**2-(N-methyl-aminomethyl)phenylboronic acid 1[^2,^3]**

![Chemical structure of 2-(N-methyl-aminomethyl)phenylboronic acid 1](image)

Tetramethylethylenediamine (181.5 mmol, 27.4 mL) (TMEDA), N-methylbenzylamine (82.5 mmol, 10.6 mL) were dissolved in 200 mL of diethyl ether in a oven-dried three-neck flask under argon. The flask was evacuated and backfilled with argon three times. *n*-Butyllithium solution (72.6 mL, 2.5 M in hexane, 181.5 mmol) was added dropwise at -78°C and reaction was refluxed for 4 h. The resulting suspension was precooled at 0°C and transferred into a vigorously stirred reaction flask containing trimethyl borate (28.11 mL, 247.5 mmol) in 100 mL of diethyl ether at -78°C. The reaction mixture was allowed to warm up to room temperature and stirring during 24 h. Solvent was evaporated and crude product was suspended in 50 mL of CH₂Cl₂ and filtered. Solvent was evaporated and brown oil obtained was distilled under reduced pressure. Colorless oil obtained was hydrolyzed in 50 mL of toluene and 20 mL of water. Toluene was evaporated and after lyophilisation, white solid was obtained (6.80 mL, 50%): mp = 189-191 °C. **¹H-NMR** (400 MHz, CDCl₃): δ = 2.10 (s, 3H), 3.47 (s, 2H), 7.04-7.09 (m, 1H), 7.23-7.27 (m, 2H), 7.68-7.72 (m, 1H); **¹³C-NMR** (400 MHz, CDCl₃): δ = 142.53, 131.46, 127.69, 127.13, 55.45, 33.03; IR (Neat): 3331, 3004, 2992, 1447, 1368, 1295, 1209, 1188, 732; HPLC (Retention time, %): 4.96 min, >99%; MS (ESI, m/z) 166.0 = (M+H)⁺

**2-(N-i-butoxycarbonyl)aminomethyl)phenylboronic acid 3[^4]**

![Chemical structure of 2-(N-i-butoxycarbonyl)aminomethyl)phenylboronic acid 3](image)

N-Boc-2-bromobenzylamine (4.0g, 14 mmol) was dissolved in THF under argon and cooled to -78°C in a oven-dried flask. The flask was evacuated and backfilled
with argon three times. MeLi (9.62 mL, 1.6 M in diethyl ether, 15.4 mmol) was added and, after 1 h, tert-Buli (17.3 mL, 1.7 M in pentane, 29.4 mmol) was added. After another 1 h, trimethyl borate (6.36 mL, 56 mmol) was added at -78°C. After warming to room temperature, the mixture was treated with dilute hydrochloric acid to pH 6 and extracted with dichloromethane. The organic phase was washed with saturated NaCl and dried with MgSO₄. The crude material was purified by column chromatography on silica gel eluting with hexanes /ethyl acetate mixture (35:65). A pale yellow solid foam was obtained (3.24g, 92%): mp = 190-192 °C. 

**1H-NMR** (400 MHz, DMSO): δ = 1.33 (s, 9H), 4.23 (d, J=6.1 Hz, 2H), 7.13 (t, J=7.3 Hz, 1H), 7.19 (d, J=7.5 Hz, 1H), 7.27 (t, J=7.5 Hz, 1H), 7.43 (d, J=7.3 Hz, 1H), 8.15 (s, 2H);

**13C-NMR** (400 MHz, CDCl₃): δ = 148.95, 131.62, 131.06, 127.13, 122.97, 82.52, 50.99, 28.61; IR (Neat): 3319, 2978, 1681, 1380, 1254, 1167, 726; HPLC (Retention time, %): 13.86 min, >99%; MS (ESI, m/z) 252.6 = (M+H)⁺

**2-(N-t-butoxycarbonyl-N-methyl)aminomethyl)phenylboronic acid 4**

2-((methylamino)methyl)phenylboronic acid (1.5 g, 9.0 mmol) was dissolved in CH₂Cl₂ and treated with Boc₂O (2.24 g, 10.3 mmol). The reaction mixture was stirred overnight at room temperature. The crude material was purified by column chromatography on silica gel eluting with a hexanes/ethyl acetate mixture (40:60). A pale yellow solid foam was obtained (1.8g, 75%): mp = 118-120 °C. 

**1H-NMR** (400 MHz, DMSO): δ = 1.36 (s, 9H), 2.69 (s, 3H), 4.51 (s, 2H), 7.02 (d, J=7.8 Hz, 1H), 7.16 (t, J=7.3 Hz, 1H), 7.30 (t, J=7.8 Hz, 1H), 7.45 (d, J=7.3 Hz, 1H), 8.11 (s, 2H);

**13C-NMR** (400 MHz, CDCl₃): δ = 157.07, 142.17, 135.12, 130.22, 128.62, 127.24, 81.16, 53.32, 28.60; IR (Neat): 3319, 2978, 1681, 1380, 1254, 1167, 726; HPLC (Retention time, %): 14.94 min, >99%; MS (ESI, m/z) 266.4 = (M+H)⁺

**N-Methyl-2-aminomethylbiphenyl 5**

Pale yellow solid: mp = 56-58 °C. 

**1H-NMR** (400 MHz, CDCl₃): δ = 2.15 (s, 3H), 2.46 (s, 1H), 3.48 (s, 2H), 7.15 (d, J=7.4 Hz, 1H), 7.23-7.42 (m, 7H), 7.49 (d, J= 7.4, 1H); 

**13C-NMR** (400 MHz, CDCl₃): δ = 142.25, 141.26, 136.26, 130.44, 129.42, 129.34, 128.52, 127.90, 127.46, 127.41, 53.23, 35.96; IR (Neat): 3323, 3057, 2932, 2843, 2789, 1478, 1449, 1007, 763, 701; HPLC (Retention time, %): 10.01 min, >99%; GC-MS (Retention time): 9.53 min; MS (ESI, m/z) 198.2 = (M+H)⁺
\textbf{N-Methyl-4'-nitro-2-aminomethylbiphenyl 6}

Yellow solid: mp = 59-61 °C \textbf{^1H-NMR} (400 MHz, CDCl$_3$): \( \delta = 1.21 \) (s, 1H), 2.37 (s, 3H), 3.64 (s, 2H), 7.25 (d, \( J=7.5 \) Hz, 1H), 7.35 (t, \( J=7.35 \) Hz, 1H), 7.41 (t, \( J=7.35 \) Hz, 1H), 7.50 (d, \( J=7.5 \) Hz, 1H), 7.61 (d, \( J=8.6 \) Hz, 2H), 8.27 (d, \( J=8.6 \) Hz, 2H); \textbf{^{13C-NMR} (400 MHz, CDCl$_3$): \( \delta =148.24, 147.30, 139.96, 136.74, 130.45, 130.03, 129.83, 128.99, 127.74, 123.68, 53.02, 36.06; IR (Neat): 3332, 2939, 2845, 2791, 1596, 1515, 1347, 1106, 855, 747; HPLC (Retention time, %): 10.48 min, >99%; GC-MS (Retention time): 14.90 min; MS (ESI, \( m/z \)) 243.0 = (M+H)$^+$

\textbf{N-Methyl-4'-methoxy-2-aminomethylbiphenyl 7}

Pale yellow oil. \textbf{^1H-NMR} (400 MHz, CDCl$_3$): \( \delta = 1.29 \) (s, 1H), 2.38 (s, 3H), 3.71 (s, 2H), 6.96 (d, \( J=8.74 \) Hz, 2H), 7.22-7.35 (m, 5H), 7.46 (d, \( J=7.35 \) Hz, 1H); \textbf{^{13C-NMR} (400 MHz, CDCl$_3$): \( \delta =159.07, 142.04, 133.44, 132.20, 130.80, 130.50, 130.27, 127.65, 128.65, 113.97, 61.19, 55.50, 45.49; IR (Neat): 3331, 2957, 2932, 2836, 1730, 1610, 1515, 1245, 1178, 1119, 835, 729; HPLC (Retention time, %): 10.40 min, >75%; GC-MS (Retention time): 12.60 min; MS (ESI, \( m/z \)) 228.2 = (M+H)$^+$

\textbf{Biphenyl-2-yl-N,N-dimethylmethanamine 8$^5$}

Colorless oil. \textbf{^1H-NMR} (400 MHz, CDCl$_3$): \( \delta = 2.23 \) (s, 6H), 3.43 (s, 2H), 7.31-7.50 (m, 8H), 7.64 (d, \( J=7.38 \) Hz, 1H); \textbf{^{13C-NMR} (400 MHz, CDCl$_3$): \( \delta =142.69, 141.69, 136.31, 130.28, 130.14, 129.86, 128.20, 127.58, 127.13, 127.05, 61.04, 45.49; IR (Neat): 3023, 2941, 2814, 2766, 1478, 1455, 1042, 762, 701; HPLC (Retention time, %): 10.13 min, >99%; GC-MS (Retention time): 9.36 min; MS (ESI, \( m/z \)) 212.3 = (M+H)$^+$

\textbf{N,N-dimethyl(4'-nitrophenyl-2-yl)methanamine 9}

Pale yellow solid: mp = 32-33 °C \textbf{^1H-NMR} (400 MHz, CDCl$_3$): \( \delta = 2.15 \) (s, 6H), 3.28 (s, 2H), 7.26 (d, \( J=7.1 \) Hz, 1H), 7.36 (t, \( J=7.4 \) Hz, 1H), 7.41 (t, \( J=7.4 \) Hz, 1H), 7.52 (d, \( J=7.5 \) Hz, 1H), 7.63 (d, \( J=8.6 \) Hz, 2H), 8.27 (d, \( J=8.6 \) Hz, 2H); \textbf{^{13C-NMR} (400 MHz, CDCl$_3$): \( \delta =148.71, 147.40, 140.58, 136.56, 130.87,}
130.75, 129.96, 128.54, 127.47, 123.34, 61.47, 45.34; IR (Neat): 2973, 2942, 2816, 2768, 1596, 1517, 1348, 855, 751; HPLC (Retention time, %): 10.57 min, >99%; GC-MS (Retention time): 14.90 min; MS (ESI, m/z) 257.2 = (M+H)^+

**(4'-methoxybiphenyl-2-yl)-N,N-dimethylmethanamine  10**

Colorless oil.\(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta = 2.19\) (s, 6H), 3.38 (s, 2H), 3.88 (s, 3H), 6.99 (d, \(J=8.6\) Hz, 2H), 7.24-7.37 (m, 5H), 7.55 (d, \(J=7.3\) Hz, 1H); \(^{13}\)C-NMR (400 MHz, CDCl\(_3\)): \(\delta = 158.87, 142.36, 136.51, 134.10, 130.94, 130.40, 130.20, 127.23, 127.00, 113.59, 61.19, 55.50, 45.49\); IR (neat): 2940, 2814, 2766, 1611, 1515, 1480, 1237, 1177, 1038, 834, 764; HPLC (Retention time, %): 10.60 min, >99%; GC-MS (Retention time): 12.30 min; MS (ESI, m/z) 242.2 = (M+H)^+

**tert-butyl biphenyl-2-ylmethylcarbamate 11**

White solid: mp = 100-101 °C \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta = 1.43\) (s, 9H), 4.28 (d, \(J=5.1\) Hz, 2H), 4.64 (br, 1H), 7.23-7.48 (m, 8H); \(^{13}\)C-NMR (400 MHz, CDCl\(_3\)): \(\delta = 155.96, 141.78, 140.98, 136.38, 130.35, 129.27, 128.61, 128.56, 128.41, 127.95, 127.46, 79.60, 42.70, 28.63\); IR (neat): 3347, 3060, 2976, 2930, 1702, 1507, 1365, 1249, 1169, 750, 703; HPLC (Retention time, %): 20.67 min, >99%; GC-MS (Retention time): 14.62 min; MS (ESI, m/z) 284.3 = (M+H)^+

**tert-butyl (4'-nitrobiphenyl-2-yl)methylcarbamate 12**

White solid: mp = 154-156 °C \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta = 1.41\) (s, 9H), 4.65 (d, \(J=5.3\) Hz, 2H), 4.65 (br, 1H), 7.23 (d, \(J=7.5\) Hz, 1H), 7.37 (t, \(J=7.5\) Hz, 1H), 7.45-7.53 (m, 4H), 8.29 (d, \(J=8.8\) Hz, 2H); \(^{13}\)C-NMR (400 MHz, CDCl\(_3\)): \(\delta = 147.83, 147.40, 139.50, 136.18, 130.25, 130.03, 129.11, 128.78, 127.85, 123.82, 79.60, 42.63, 28.57\); IR (neat): 3340, 2979, 2934, 1689, 1511, 1350, 178, 750; HPLC (Retention time, %): 20.13 min; GC-MS (Retention time): 19.33 min, >99%; MS (ESI, m/z) 329.4 = (M+H)^+
**tert-butyl (4'-methoxybiphenyl-2-yl)methylcarbamate 13**

White solid: mp = 65-66 °C. $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ = 1.44 (s, 9H), 3.86 (s, 3H), 4.29 (d, $J$=5.3 Hz, 2H), 4.66 (br, 1H), 6.96 (d, $J$=8.6 Hz, 2H), 7.20-7.37 (m, 5H), 7.44 (d, $J$=7.1 Hz, 1H); $^{13}$C-NMR (400 MHz, CDCl$_3$): $\delta$ = 159.09, 155.96, 141.46, 136.51, 133.33, 130.52, 130.35, 128.42, 127.68, 127.44, 114.00, 79.58, 55.60, 42.76, 28.63; IR (neat): 3349, 2975, 2932, 1701, 1515, 1244, 1172, 722; HPLC (Retention time, %): 20.45 min, >99%; GC-MS (Retention time): 17.23 min; MS (ESI, m/z) 314.3 = (M+H)$^+$

**tert-butyl biphenyl-2-ylmethyl(methyl)carbamate 14**

Colorless oil. $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ = 1.44 (s, 4.5H), 1.50 (s, 4.5H), 2.65 (s, 1.5H), 2.73 (s, 1.5H), 4.41 (s, 1H), 4.49 (s, 1H) 7.24-7.40 (m, 9H); $^{13}$C-NMR (400 MHz, CDCl$_3$ t=50ºC): $\delta$ = 156.21, 141.91, 141.17, 135.56, 130.23, 129.40, 128.50, 127.94, 127.40, 127.17, 127.05, 79.69, (50.5, 49.7) , 34.15, 28.66; IR (neat): 3060, 2975, 2930, 1693, 1478, 1451, 1391, 1146, 751; HPLC (Retention time, %): 23.17 min, >99%; GC-MS (Retention time): 14.68 min; MS (ESI, m/z) 298.4 = (M+H)$^+$

**tert-butyl methyl((4'-nitrobenzopyrene-2-yl)methyl)carbamate 15**

White solid: mp = 78-79 °C. $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ = 1.40 (s, 9H), 2.61 (s, 1.5H), 2.71 (s, 1.5H), 4.36 (s, 1H), 4.43 (s, 1H) 7.21 (d, $J$=7.3 Hz, 1H), 7.29-7.50 (m, 5H), 8.28 (d, $J$=8.3 Hz, 2H); $^{13}$C-NMR (400 MHz, CDCl$_3$ t=50ºC): $\delta$ = 156.09, 147.95, 147.34, 139.48, 135.40, 130.22, 130.00, 129.10, 128.18, 127.53, 123.77, 80.05, (50.44, 49.87), 34.22, 28.57; IR (neat): 3065, 2976, 2930, 1692, 1597, 1478, 1391, 1148, 855, 751; HPLC (Retention time, %): 22.09 min, >99%; GC-MS (Retention time): 19.84 min; MS (ESI, m/z) 343.3 = (M+H)$^+$

**tert-butyl (4'-methoxybiphenyl-2-yl)methyl(methyl)carbamate 16**

White solid: mp = 59-61 °C. $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ = 1.42 (s, 4.5H), 1.46 (s, 4.5H), 2.62 (s, 1.5H), 2.72 (s, 1.5H), 4.39 (s, 1H), 4.46 (s, 1H) 6.95 (d, $J$=7.3 Hz, 2H), 7.20-7.34 (m, 6H); $^{13}$C-NMR (400 MHz, CDCl$_3$ t=50ºC): $\delta$ = 159.12, 156.37, 141.53, 135.60, 133.53, 130.40, 127.57, 126.92, 126.99,
113.96, 79.66, (55.48, 55.57), (50.48, 49.70), 34.30, 28.63; IR (neat): 2932, 2974, 1693, 1479, 1391, 1244, 1146, 1117, 762; HPLC (Retention time, %): 22.70 min, >99%; GC-MS (Retention time): 17.26 min; MS (ESI, m/z) 328.4 = (M+H)+

NMR Spectra

General procedure for $^{11}$B NMR studies of compounds 3 and 4 in toluene

A solution of compound 3 or 4 (1mL 0.12M in Toluene-d8) was prepared and used to record the first spectrum. Subsequently, aliquots of 10µL of aqueous NaOH (1N) were added to the tube and spectra were recorded. The temperature was regulated at 22°C.

![NMR Spectra](image)

Figure 1. $^{11}$B NMR spectra of compound 3 in Toluene-d8 (0.12M) with a varying addition of NaOH 1N.
S14
**10**

The diagram shows the 1H NMR spectra of two compounds, each labeled as 10.

The spectra are labeled with PPM values across the x-axis, ranging from 0 to 180.

The spectra include chemical shifts and other data points, indicating the chemical structures present in the samples.
file: C:\Documents and Settings\Pierre-Luc\Mes documents\Docto ra\RMN\RMN\PLUC93_26 Sep 2006\PROTON_01.fid\fid block #1 expect: "s2pul"
transmitter freq.: 399.775827 MHz
time domain size: 47896 points
width: 6396.42 Hz = 16.00012 ppm = 0.133548 Hz/pt
number of scans: 16
freq. of 0 ppm: 399.773429 MHz
processed size: 65536 complex points
LB: 0.000 GB: 0.000

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transmitter freq.: 100.534142 MHz
time domain size: 60288 points
width: 25133.52 Hz = 249.999864 ppm = 0.416891 Hz/pt
number of scans: 256
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transmitter freq.: 399.775827 MHz
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number of scans: 16

freq. of 0 ppm: 399.773429 MHz
processed size: 65536 complex points
LB: 0.000     GB: 0.0000

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transmitter freq.: 100.534142 MHz
time domain size: 60288 points
width: 25133.52 Hz = 249.999864 ppm = 0.416891 Hz/pt
number of scans: 256

freq. of 0 ppm: 100.523085 MHz
processed size: 65536 complex points
LB: 1.000     GB: 0.0000

16

N Boc

OMe

S22
HPLC Chromatograms

Intensity/Time (minutes)

Intensity/Time (minutes)

Intensity/Time (minutes)
Intensity/Time (minutes)
Intensity/Time (minutes)

Intensity/Time (minutes)

Intensity/Time (minutes)
References


