Supplementary Information

Mesityllithium and p-(dimethylamino)phenyllithium
for the selective alternate trilithiation of the hexaphenylbenzene framework

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Contents

• General information and materials ................................................. S2
• Preparation of HPB derivative 5f .................................................. S2
• Selective alternate trilithiation of compound 1 with in situ prepared MesLi or MapLi ................................................................. S3
• Selective alternate trilithiation of compounds 5a-f with in situ prepared MesLi S3
• Large-scale synthesis of compounds 4 and 6c with granular lithium and MapBr S4
• Attempted alternate trilithiation of compound 1 with PhLi .................... S5
• Equilibration experiments with MesLi and MapLi ............................. S6
• Confirmation of the in situ preparation of MesLi ............................. S7
• Attempted alternate trilithiation of compound 1 with in situ prepared PhLi and p-CF₃C₆H₄Li ............................................................... S8
• Attempted lithiation of compound 1 with excess amount of MesLi or MapLi S9
• References .................................................................................. S9
• ¹H and ¹³C NMR spectra ............................................................... S10
General Information

$^1$H NMR and $^{13}$C NMR spectra were recorded with tetramethylsilane as the internal standard using a Bruker AV-500 (500 MHz) spectrometer. High-resolution mass spectra (HRMS) were obtained using a Waters Xevo G2 Tof mass spectrometer. Melting points were determined using a SCINICS SMP-300 instrument.

Materials

Unless otherwise noted, all solvents and reagents were obtained from commercial suppliers (TCI Co., Ltd., WAKO Pure Chemical Industries Ltd., KANTO Chemical Co., Ltd., and Sigma-Aldrich Co.) and were used as received. Compounds $^1$1, $^1$5a-e, $^2$4-iodo-$N,N$-dimethylaniline ($^7$) $^3$and tetracyclone ($^8$) $^4$ were prepared according to the literature.

Preparation of compound 5f

Scheme S1. Preparation of compound 5f.

To the solution of compound 7 ($3.00$ g, 12.1 mmol), Pd($PPh_3)_2Cl_2$ (169 mg, 2 mol%), CuI (46 mg, 2 mol%) in degassed NEt₃ (25 mL) was added trimethylsilylacetylene (1.73 mL, 12.1 mmol) at rt. The solution was stirred for 1 h at 50 °C. To the mixture were then added $p$-bromiodobenzene (3.77 g, 13.3 mmol) and the methanol solution of KOH (0.55 g/mL, 8 mL). The mixture was vigorously stirred for 2 h at 50 °C. Then the solvent was removed in vacuo. After the addition of aq. NH₄Cl (20 mL) and CH₂Cl₂ (100 mL), the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (20 mL × 3) and the combined extracts were dried over anhydrous MgSO₄ and filtered. The concentration of the solution in vacuo resulted in the precipitation, which was collected by filtration to afford compound 9 (2.59 g, 71%) as a brown solid.

9: m.p. 145-146 °C; $^1$H NMR (500 MHz, CDCl₃, 298 K) δ 7.44 (d, $J = 9.0$ Hz, 2H), 7.39 (d, $J = 9.0$ Hz, 2H), 7.35 (d, $J = 9.0$ Hz, 2H), 6.66 (d, $J = 9.0$ Hz, 2H), 3.00 (s, 6H); $^{13}$C $^1$H NMR (126 MHz, CDCl₃, 298 K) δ 150.36, 132.87, 132.82, 131.59, 123.32, 121.58, 111.94, 109.70, 92.03, 86.52, 40.33 (11 signals); HRMS (ASAP) Calcd for [M+H]$^+$ C$_{16}$H$_{23}$BrN 300.0388, found 300.0392.

The mixture of compound 9 (0.708 g, 2.36 mmol) and tetracyclone (1.50 g, 2.14 mmol) in degassed Ph₂O (2 mL) was stirred at 235 °C for 2.5 h. To the mixture was then added compound 9 (0.211 g, 0.703 mmol). The mixture was again stirred at 235 °C for 2.5 h. After cooling to rt and the addition of Et₂O (2 mL), the resulting
precipitation was filtered and thoroughly washed with Et₂O to afford compound 5f (1.33 g, 64%) as a flesh-colored solid.

5f: m.p. >300 °C; ¹H NMR (500 MHz, CDCl₃, 298 K) δ 7.05-7.02 (m, 10H), 6.64-6.60 (m, 10H), 6.52 (d, J = 9.0 Hz, 2H), 6.25 (d, J = 9.0 Hz, 2H), 2.80 (s, 6H); ¹³C{¹H} NMR (126 MHz, CDCl₃, 298 K) δ 148.46, 141.33, 140.15, 139.40, 139.36, 139.08, 138.96, 138.67, 132.96, 132.86, 132.85, 131.90, 130.46, 130.45, 130.27, 127.19, 120.22, 120.19, 119.86, 111.35, 40.47 (21 signals); HRMS (ASAP) Calcd for [M+H]+ C₄₄H₃₇Br₃81N 971.8337, found 971.8332.

Selective alternate trilithiation of compound 1 with in situ prepared MesLi or MapLi

To the suspension of compound 1 (0.200 g, 0.198 mmol) and MesBr (84 µL, 0.55 mmol) in THF (2 mL) was added the freshly titrated pentane solution of t-BuLi (1.68 M, 0.708 mL, 1.19 mmol) at –98 °C. After removal of the cooling bath, the reaction mixture was stirred for 30 min, and then quenched by the addition of TMSCl (0.151 mL, 1.19 mmol) at –98 °C. After the addition of water (10 mL) and CHCl₃ (10 mL), the organic layer was separated. The aqueous layer was extracted with CHCl₃ (10 mL × 3) and the combined extracts were washed over anhydrous MgSO₄, and filtered. Then the solvent was removed in vacuo and recrystallization from CHCl₃/EtOH afforded compound 4 (0.129 g, 66%) as a colorless solid.

To the suspension of compound 1 (0.200 g, 0.198 mmol) and MapBr (0.111 g, 0.555 mmol) in THF (2 mL) was added the freshly titrated pentane solution of t-BuLi (1.68 M, 0.708 mL, 1.19 mmol) at –98 °C. After removal of the cooling bath, the reaction mixture was stirred for 30 min, and then quenched by the addition of TMSCl (0.151 mL, 1.19 mmol) at –98 °C. After the addition of water (10 mL) and CHCl₃ (10 mL), the organic layer was separated. The aqueous layer was extracted with CHCl₃ (10 mL × 3) and the combined extracts were washed twice with aq.HCl (1 M). The resulting organic solution was dried over anhydrous MgSO₄, and filtered. Then the solvent was removed in vacuo and recrystallization from CHCl₃/EtOH afforded compound 4 (0.124 g, 63%) as a colorless solid.

Selective alternate trilithiation of compounds 5a-f with in situ prepared MesLi

To the suspension of pentabrominated HPB derivatives 5a-f (5a: 0.200 g, 5b: 0.200 g, 5c: 0.150 g, 5d: 0.150 g, 5e: 0.150 g, 5f: 0.200 g,) and MesBr (2.8 equiv.) in THF (2 mL) was added the freshly titrated pentane solution of t-BuLi (6 equiv.) at –98 °C. After removal of the cooling bath, the reaction mixture was stirred for 30-40 min. Then the reaction was quenched by the addition of TMSCl (6 equiv.) at –98 °C. After the addition of aq. NH₄Cl (10 mL) and CHCl₃ (10 mL), the organic layer was separated. The aqueous layer was extracted with CHCl₃ (10 mL × 3) and the combined extracts were washed twice with aq.HCl (1 M). The resulting organic solution was dried over anhydrous MgSO₄, and filtered. Then the solvent was removed in vacuo and recrystallization from CHCl₃/EtOH afforded compounds 6a-f (6a: 128 mg (65%), 6b: 149 mg (76%), 6c: 80 mg (54%), 6d: 98 mg, (67%), 6e: 88 mg (60%), 6f: 114 mg (58%)) as a colorless solid.

The spectroscopic data of 6a and 6b were in agreement with those reported in the literature.[²]

S3
6c: m.p. 296-299 °C; \(^1^H\) NMR (500 MHz, CDCl\(_3\), 298 K) \(\delta\) 7.03 (d, \(J = 8.2\) Hz, 2H), 7.00 (d, \(J = 8.2\) Hz, 4H), 6.95 (d, \(J = 8.6\) Hz, 4H), 6.84-6.80 (m, 3H), 6.77-6.74 (m, 2H), 6.73 (d, \(J = 8.2\) Hz, 4H), 6.73 (d, \(J = 8.2\) Hz, 2H), 6.64 (d, \(J = 8.6\) Hz, 4H), 0.14 (s, 9H), 0.11 (s, 18H); \(^{13}\)C \(^1^H\) NMR (126 MHz, CDCl\(_3\), 298 K) \(\delta\) 140.75, 140.70, 140.64, 140.49, 140.29, 140.26, 139.65, 139.24, 137.52, 137.21, 133.13, 131.99, 131.81, 131.45, 130.73, 129.84, 126.69, 125.31, 119.50, –1.03, –1.06 (21 signals; One signal in an aromatic region was not observed because of overlapping.); HRMS (ASAP) Calcd for [M]+ C\(_{9}\)H\(_{52}\)Br\(_{3}\)S\(_{9}\) 906.1744, found 906.1756.

6d: m.p. >300 °C; \(^1^H\) NMR (500 MHz, CDCl\(_3\), 298 K) \(\delta\) 7.02 (d, \(J = 8.2\) Hz, 2H), 7.00 (d, \(J = 8.2\) Hz, 4H), 6.94 (d, \(J = 8.6\) Hz, 4H), 6.73 (d, \(J = 8.2\) Hz, 4H), 6.72 (d, \(J = 8.2\) Hz, 2H), 6.63 (d, \(J = 8.6\) Hz, 4H), 6.62 (s, 4H), 2.08 (s, 3H) 0.14 (s, 9H), 0.12 (s, 18H); \(^{13}\)C \(^1^H\) NMR (126 MHz, CDCl\(_3\), 298 K) \(\delta\) 140.85, 140.80, 140.71, 140.54, 140.08, 139.72, 139.19, 137.46, 137.16, 137.07, 134.57, 133.13, 131.97, 131.78, 131.29, 130.74, 129.81, 127.38, 119.45, 21.08, –1.04 (21 signals; One signal in an aromatic region and one signal from TMS group were not observed because of overlapping.); HRMS (ASAP) Calcd for [M]+ C\(_{9}\)H\(_{52}\)Br\(_{3}\)S\(_{9}\) 920.1900, found 920.1909.

6e: m.p. 286-289 °C; \(^1^H\) NMR (500 MHz, CDCl\(_3\), 298 K) \(\delta\) 7.02 (d, \(J = 8.2\) Hz, 2H), 7.02 (d, \(J = 8.2\) Hz, 4H), 6.94 (d, \(J = 8.5\) Hz, 4H), 6.73 (d, \(J = 8.2\) Hz, 4H), 6.72 (d, \(J = 8.2\) Hz, 2H), 6.65 (d, \(J = 8.9\) Hz, 2H), 6.63 (d, \(J = 8.5\) Hz, 4H), 6.37 (d, \(J = 8.9\) Hz, 2H), 3.60 (s, 3H), 0.14 (s, 9H), 0.12 (s, 18H); \(^{13}\)C \(^1^H\) NMR (126 MHz, CDCl\(_3\), 298 K) \(\delta\) 157.22, 140.98, 140.83, 140.53, 140.28, 140.12, 139.72, 139.24, 137.48, 137.11, 133.13, 132.72, 132.50, 131.98, 131.87, 130.78, 129.82, 119.47, 112.31, 55.15, –1.03 (22 signals; One signal from TMS group was not observed because of overlapping.); HRMS (ASAP) Calcd for [M]+ C\(_{9}\)H\(_{52}\)Br\(_{3}\)S\(_{9}\)O 936.1849, found 936.1843.

6f: m.p. 254 °C (dec.); \(^1^H\) NMR (500 MHz, CDCl\(_3\), 298 K) \(\delta\) 7.02 (d, \(J = 8.2\) Hz, 4H), 7.02 (d, \(J = 8.2\) Hz, 2H), 6.94 (d, \(J = 8.2\) Hz, 4H), 6.74 (d, \(J = 8.2\) Hz, 4H), 6.72 (d, \(J = 8.2\) Hz, 2H), 6.63 (d, \(J = 8.2\) Hz, 2H), 6.56 (d, \(J = 8.8\) Hz, 4H), 6.22 (d, \(J = 8.8\) Hz, 2H), 2.72 (s, 6H), 0.14 (s, 9H), 0.12 (s, 18H); \(^{13}\)C \(^1^H\) NMR (126 MHz, CDCl\(_3\), 298 K) \(\delta\) 148.37, 141.13 141.04, 140.83, 140.67, 139.90, 139.74, 139.15, 137.35, 136.78, 133.18, 132.19, 131.93, 131.81, 130.87, 130.79, 129.77, 128.75, 119.37, 111.57, 40.80, –1.02 (22 signals; One signal from TMS group was not observed because of overlapping.); HRMS (ASAP) Calcd for [M+H]+ C\(_{9}\)H\(_{58}\)Br\(_{3}\)NSi\(_{3}\) 950.2244, found 950.2244.

**Large-scale synthesis of compounds 4 and 6c from granular lithium and MapBr**

To granular lithium (1.86 g, 0.268 mol) was added the solution of MapBr (26.8 g, 0.134 mol) in Et\(_2\)O (100 mL) dropwise in 10 min. During the addition, the solution spontaneously refluxed. After the addition, the mixture was refluxed for 1 h. Then THF (200 mL) and compound 1 (30.0 g, 29.8 mmol) was added at 0 °C. The mixture was stirred for 20 min at 0 °C and transferred to another reaction vessel containing TMSCl (34.0 mL, 0.268 mol) at 0 °C. Then the solvent was removed in vacuo. After the addition of water (100 mL) and CHCl\(_3\) (100 mL), the organic layer was separated. The aqueous layer was extracted with CHCl\(_3\) (100 mL × 3) and the combined extracts were washed twice with aq.HCl (1 M). The resulting organic solution was dried over anhydrous MgSO\(_4\), and filtered. Then the solvent was removed in vacuo and recrystallization from CHCl\(_3\)/EtOH afforded compound 4 (19.5 g, 66%) as a colorless solid.
To granular lithium (0.556 g, 80.1 mmol) was added the solution of MapBr (8.02 g, 40.1 mmol) in Et₂O (25 mL) dropwise in 10 min. During the addition, the solution spontaneously refluxed. Then the mixture was refluxed for 1 h. Then THF (50 mL) and compound 5c (8.27 g, 8.90 mmol) was added at 0 °C. The mixture was stirred for 20 min at 0 °C. To the resulted solution was then added TMSCl (10.2 mL, 80.1 mmol) at 0 °C, and the solvent was removed in vacuo. After the addition of water (50 mL) and CHCl₃ (50 mL), the organic layer was separated. The aqueous layer was extracted with CHCl₃ (50 mL × 3) and the combined extracts were washed twice with aq.HCl (1 M). The resulting organic solution was dried over anhydrous MgSO₄, and filtered. Then the solvent was removed in vacuo and recrystallization from CHCl₃/EtOH (twice) afforded compound 6c (3.87 g, 48%) as a colorless solid.

**Attempted alternate trilithiation of compound 1 with PhLi**

To the suspension of compound 1 (0.200 g, 0.198 mmol) in THF (2 mL) was added the diethyl ether and cyclohexane solution of PhLi (1.07 M, 0.556 mL, 0.594 mmol) at 0 °C. The reaction mixture was stirred at rt for 20 min, and then quenched by the addition of TMSCl (0.15 mL, 1.2 mmol) at –98 °C. After the addition of water and CHCl₃, the organic layer was analyzed by ¹H NMR spectroscopy.

![Figure S1](image)

**Figure S1.** Partial ¹H NMR spectra (500 MHz, CDCl₃, 298 K) of the crude mixture obtained in the lithiation of compound 1 with a) t-BuLi (6 equiv.) or b) PhLi (3 equiv.).
**Equilibration experiments with MesLi and MapLi**

To the solution of Ar\(^3\)Br (1.3 mmol) in THF (4 mL) was added the pentane solution of \(\text{t-BuLi}\) (2.6 mmol) at –98 °C. After removal of the cooling bath, the solution was stirred for 20 min. Then Ar\(^3\)Br (1.3 mmol) was added to the solution, and the mixture was stirred at rt for 10 min. Then the reaction mixture was quenched with benzaldehyde (0.20 mL). After the addition of aq.NH\(_4\)Cl (10 mL), the product was extracted with CH\(_2\)Cl\(_2\) (10 mL \(\times\)3). The combined organic extracts were dried over anhydrous MgSO\(_4\) and filtered. Then the solvent was removed in vacuo and \(^1\)H NMR yields of the benzhydrol derivatives were determined with CHCl\(_3\)/CHCl\(_3\) as an internal standard.

**Scheme S2.** Comparison of the relative thermodynamic stability of PhLi, MesLi and MapLi as an aryllithium by equilibration experiments.
Confirmation of the in situ preparation of MesLi

The in situ preparation of MesLi was confirmed by the comparison of the crude product obtained by the rapid quenching of the lithiation reaction of compound 1 in the absence or the presence of MesBr. While three equivalents of lithiation of substrate 1 were completed in the absence of MesBr in 2.5 min after removal of the cooling bath, almost all of substrate 1 remained unreacted in the presence of MesBr in 2.5 min. This should be due to the selective lithiation of MesBr by t-BuLi.

Figure S2. Partial $^1$H NMR spectra (500 MHz, CDCl$_3$, 298 K) of the crude mixture obtained by quenching with TMSCl 2.5 min after removal of the cooling bath a) in the absence of MesBr, b) in the presence of MesBr.
Attempted alternate trilithiation of compound 1 with \textit{in situ} prepared PhLi and \( p\text{-CF}_3\text{C}_6\text{H}_4\text{Li} \)

To the suspension of compound 1 (0.200 g, 0.198 mmol) and ArBr (2.8 equiv.) in THF (2 mL) was added the freshly titrated pentane solution of \( t\text{-BuLi} \) (1.74 M, 0.684 mL, 1.19 mmol) at \(-98 \) °C. After removal of the cooling bath, the reaction mixture was stirred for 30 min, and then quenched by the addition of TMSCl (0.151 mL, 1.19 mmol) at \(-98 \) °C. After the addition of water (10 mL) and CHCl$_3$ (10 mL), the organic layer was analyzed by \(^1\)H NMR spectroscopy.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure.png}
\caption{Partial \(^1\)H NMR spectra (500 MHz, CDCl$_3$, 298 K) of the crude mixture obtained with various kinds of \textit{in situ} prepared ArLi reagents: a) MesBr, b) MapBr, c) PhBr, d) \( p\text{-CF}_3\text{C}_6\text{H}_4\text{Br} \).}
\end{figure}
Attempted lithiation of compound 1 with excess amount of MesLi or MapLi

To the suspension of compound 1 (0.200 g, 0.198 mmol) and ArBr (4.5 equiv.) in THF (2 mL) was added the freshly titrated pentane solution of t-BuLi (1.82 M, 0.981 mL, 1.79 mmol) at –98 °C. After removal of the cooling bath, the reaction mixture was stirred for 30 min, and then quenched by the addition of TMSCl (0.151 mL, 1.19 mmol) at –98 °C. After the addition of water (10 mL) and CHCl₃ (10 mL), the organic layer was analyzed by ¹H NMR spectroscopy. As for the reaction with MapBr, the organic layer was washed twice with aq. HCl (1 M), dried over anhydrous MgSO₄, and filtered. Then the solvent was removed in vacuo and recrystallization from CHCl₃/EtOH afforded compound 4 (0.128 g, 65%) as a colorless solid.

![Figure S4. Partial ¹H NMR spectra (500 MHz, CDCl₃, 298 K) of the crude mixture obtained with 4.5 equiv. of a) MapLi or b) MesLi.](image)

References
H and C NMR spectra
The image contains a chemical structure labeled as 6e. The structure includes a central carbon ring with multiple substituents: an OMe group, a Br group, and TMS groups. The spectrum on the right side of the image shows various chemical shifts, with peaks at different ppm values.
S20

NMe₂

6f