Versatile, mild, and selective reduction of various carbonyl groups using an electron-deficient boron catalyst

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1. General Methods

Reagent chemicals were obtained from commercial sources and used without further purification. Flash chromatography was performed with columns of 40–63 Å silica gel, 230–400 mesh (Silicycle, Québec City, Canada). Thin-layer chromatography (TLC) was performed on plates of EMD 250-μm silica 60-F254. The phrase “concentrated under reduced pressure” refers to the removal of solvents and other volatile materials using a rotary evaporator while maintaining the water-bath temperature below 40 °C. Residual solvent was removed from samples at high vacuum (<0.1 torr). The term “high vacuum” refers to vacuum achieved by mechanical a belt-drive oil pump. All NMR spectra were acquired at ambient temperature with a Bruker Ultra Shield Plus 400, and were referenced to TMS or a residual protic solvent.

Electrospray ionization (ESI) mass spectrometry for small-molecule characterization was performed with a Micromass LCT at the Mass Spectrometry Facility in the Department of Chemistry at the University of Wisconsin–Madison. {NIH 1S10OD020022-1}

2. Experimental Procedures and Characterization Data

4-Methoxytoluene

\[
\begin{align*}
  \text{H} & \text{-} \text{O} \\
  \text{H} & \text{-} \text{O} \\
  \text{Et}_3\text{SiH} & \text{B(C}_6\text{F}_5) \text{H} \\
  \text{CH}_2\text{Cl}_2 & \rightarrow \\
  \text{H} & \text{-} \text{O} \\
  \text{H} & \text{-} \text{O} \\
\end{align*}
\]

\(p\)-Anisaldehyde (0.055 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.19 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 4-Methoxytoluene (0.039 g, 79%).

$^1$H NMR (400 MHz, CDCl$_3$) \(\delta\ 7.01\ (d, J=8.3\ Hz, 2H), 6.74\ (d, J=8.3\ Hz, 1H), 3.78\ (s, 3H), 2.27\ (s, 3H)\).

*Checked against Sigma-Aldrich: http://www.sigmaaldrich.com/spectra/fnmr/FNMR001412.PDF

4-Ethylanisole

\[
\begin{align*}
  \text{O} & \rightarrow \\
  \text{O} & \rightarrow \\
  \text{Et}_3\text{SiH} & \text{B(C}_6\text{F}_5) \text{H} \\
  \text{CH}_2\text{Cl}_2 & \rightarrow \\
  \text{O} & \rightarrow \\
  \text{O} & \rightarrow \\
\end{align*}
\]
p-Methoxyacetophenone (0.061 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.19 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 4-Ethylanisole (0.042 g, 75%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \text{)} \delta 7.12 (d, J = 8.6 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 3.79 (s, 3H), 2.59 (q, J = 7.6 Hz, 2H), 1.21 (t, J = 7.6 Hz, 3H). \]


2-Methoxy-4-methylphenol

Vanillin (0.062 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.13 mL, 0.818 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 2-Methoxy-4-methylphenol (0.044 g, 78%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \text{)} \delta 6.81 (d, J = 7.8 Hz, 1H), 6.70 – 6.61 (m, 3H), 5.42 (s, 1H), 3.87 (s, 3H), 2.29 (s, 3H). \]

*Checked against Sigma-Aldrich: http://www.sigmaaldrich.com/spectra/fnmr/FNMR006218.PDF

4-Trifluoromethyl-N-ethylaniline

4-Trifluoromethylacetanilide (0.083 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.2 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 4-Trifluoromethyl-N-ethylaniline (0.070 g, 91%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \text{)} \delta 7.39 (d, J = 8.1 Hz, 2H), 6.58 (d, J = 8.1 Hz, 2H), 3.89 (bs, 1H), 3.25 – 3.12 (m, 2H), 1.27 (t, J = 7.2 Hz, 3H). \]

*13C NMR (101 MHz, CDCl3) δ 150.7, 126.6 (q, J = 3.9 Hz), 125.0 (q, J = 270.4 Hz), 118.5 (q, J = 32.6 Hz), 111.7, 38.0, 14.6. Corrected 13C-NMR spectral data from incorrect data in: Sajiki, H. *Org. Lett.* 2004, 6, 4977-4980. Authors might not have realized that F is a spin active nucleus

4-Methoxy-N-ethylaniline
4-Methoxy-N-Acetylaniline (0.067 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.20 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (1.050 g, 0.204 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 4-Methoxy-N-ethylaniline (0.051 g, 82%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 6.79 (d, $J$ = 8.9 Hz), 6.63 (d, $J$ = 8.9 Hz), 3.76, 3.12 (q, $J$ = 7.1 Hz), 1.23 (t, $J$ = 7.1 Hz).


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4-Trifluoromethoxy-N-ethylaniline

4-(Trifluoromethoxy)-N-Acetylaniline (0.086 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.20 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 4-Trifluoromethoxy-N-ethylaniline (0.054 g, 87%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.03 (d, $J$ = 9.0 Hz, 2H), 6.55 (d, $J$ = 9.0 Hz, 2H), 3.61 (bs, 1H), 3.17 – 3.09 (m, 2H), 1.26 (t, $J$ = 7.1 Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 147.2, 140.2, 122.4, 120.7 (q, $J$ = 255.6 Hz), 112.8, 38.6, 14.8.

---

N-Ethylaniline

Acetanilide (0.055 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.20 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield N-Ethylaniline (0.046 g, 94%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.18 (t, $J$ = 7.5 Hz, 2H), 6.70 (t, $J$ = 7.5 Hz, 1H), 6.61 (d, $J$ = 7.5 Hz, 2H), 3.61 (bs, 1H), 3.55 (bs, 1H), 3.16 (q, $J$ = 7.2 Hz, 2H), 1.26 (t, $J$ = 7.2 Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 129.2, 117.2, 112.7, 38.5, 14.9. HRMS (ESI) m/z 122.0963 [calc’d for C$_8$H$_{11}$N (M+H$^+$) 122.0964].
N-Methyl-N-ethylaniline

\[
\begin{align*}
\text{N-Methylacetanilide} & \quad (0.061 \text{ g}, 0.409 \text{ mmol}) \text{ was dissolved in dichloroethane (4.1 mL) in a scintillation vial. Triethylsilane (0.33 mL, 2.045 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir at 60°C for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield N-Methyl-N-ethylaniline (0.041 g, 74%).}
\end{align*}
\]

\[\text{^1H NMR (400 MHz, CDCl}_3\text{)} \delta 7.23 (dd, J = 9.1, 7.6 Hz, 2H), 6.79 – 6.59 (m, 3H), 3.40 (q, J = 7.1 Hz, 2H), 2.90 (s, 3H), 1.12 (t, J = 7.1 Hz, 2H). \text{^13C NMR (101 MHz, CDCl}_3\text{)} \delta 149.1, 129.2, 116.0, 112.4, 46.8, 37.5, 11.2. \text{HRMS (ESI) } m/z 136.1120 \text{ [calc'd for C}_9\text{H}_{13}\text{N (M+H}^+\text{) 136.1121].}\]

4-Ethylaminoacetophenone

\[
\begin{align*}
\text{4-(Acetamido)acetophenone} & \quad (0.072 \text{ g}, 0.409 \text{ mmol}) \text{ was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.20 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 4-(Ethylamino)acetophenone (0.058 g, 88%).}
\end{align*}
\]

\[\text{^1H NMR (400 MHz, CDCl}_3\text{)} \delta 7.39 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.3 Hz, 2H), 2.61 (q, J = 7.6 Hz, 2H), 2.16 (s, 3H), 1.21 (t, J = 7.6 Hz, 3H). \text{^13C NMR (101 MHz, CDCl}_3\text{)} \delta 168.1, 140.4, 135.5, 128.3, 120.1, 28.3, 24.5, 15.6 \text{ HRMS (ESI) } m/z 164.1070 \text{ [calc'd for C}_{10}\text{H}_{13}\text{NO (M+H}^+\text{) 164.1070].}\]

Ethyl-4-ethylaminobenzoate

\[
\begin{align*}
\text{Ethyl-4-(acetamido)benzoate} & \quad (0.085 \text{ g}, 0.409 \text{ mmol}) \text{ was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.20 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g,}
\end{align*}
\]

--S4--
0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield Ethyl-4-(ethylamino)benzoate (0.069 g, 87%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.87 (d, $J = 8.8$ Hz, 2H), 6.54 (d, $J = 8.8$ Hz, 2H), 4.31 (q, $J = 7.1$ Hz, 2H), 3.22 (q, $J = 7.2$ Hz, 2H), 1.36 (t, $J = 7.1$ Hz, 3H), 1.28 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.9, 151.9, 131.4, 118.5, 111.3, 60.2, 37.9, 14.6, 14.5. HRMS (ESI) $m/z$ 194.1176 [calc'd for C$_{11}$H$_{15}$NO$_2$ (M+H$^+$) 194.1176].

**Inhibitory Study:**

![Chemical diagram](diagram)

4-Trifluoromethylacetanilide (0.083 g, 0.409 mmol) and N-acetyldiisobutylamine (0.070 g, 0.409 mmol) were dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.67 mL, 4.09 mmol) was then added followed by tris(pentafluorophenyl)borane (0.315 g, 0.614 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 4-Trifluoromethyl-N-ethylaniline (0.037 g, 48%). Without the molar excess of borane, no product formation was observed.

Characterization Data: See Above

**2-(4’-Methylcarboxylate)-N,N-bis(triethylsilyl)phenethylamine**

![Chemical diagram](diagram)

Methyl 4-(cyanomethyl) benzoate (0.071 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.19 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 2-(4’-Methoxy)-N,N-bis(triethylsilyl)phenethylamine (0.139 g, 84%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.96 (d, $J = 8.2$ Hz, 2H), 7.21 (d, $J = 8.2$ Hz, 2H), 3.90 (s, 3H), 3.05 – 2.85 (m, 2H), 2.78 – 2.64 (m, 2H), 0.98 (t, $J = 7.9$ Hz, 18H), 0.68 (q, $J = 7.9$ Hz, 12H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 167.1, 145.7, 129.8, 128.5, 128.0, 52.0, 47.6, 42.5, 7.6, 5.7. HRMS (ESI) $m/z$ 408.2745 [calc’d for C$_{22}$H$_{41}$NO$_2$Si$_2$ (M+H$^+$) 408.2749]
2-(4’-Methoxy)-N,N-bis(triethylsilyl)phenethylamine

\[
\text{MeO} \quad \text{Et}_3\text{SiH} \quad \text{B}(\text{C}_6\text{F}_5)_3 \quad \text{MeO} \quad \text{TES} \quad \text{TES}
\]

4-Methoxyphenylacetonitrile (0.060 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.19 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 2-(4’-Methoxy)-N,N-bis(triethylsilyl)phenethylamine (0.128 g, 83%).

\[\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.08 (d, J = 8.6 \text{ Hz}, 2\text{H}), 6.83 (d, J = 8.6 \text{ Hz}, 2\text{H}), 3.79 (s, 3\text{H}), 2.97 – 2.82 (m, 2\text{H}), 2.65 – 2.54 (m, 2\text{H}), 0.97 (t, J = 7.9 \text{ Hz}, 18\text{H}), 0.67 (q, J = 7.9 \text{ Hz}, 12\text{H}).\]

\[\text{13C NMR (101 MHz, CDCl}_3\text{)} \delta 157.9, 132.4, 129.4, 113.8, 55.2, 48.2, 41.4, 7.6, 5.7.\]

\[\text{HRMS (ESI) } m/z 380.2793 \text{ [calc’d for } \text{C}_{21}\text{H}_{41}\text{NOSi}_2 (\text{M}+\text{H}^+) \text{ 380.2799}.}\]

4-Ethylaminophenylacetonitrile

\[
\text{O} \quad \text{Et}_3\text{SiH} \quad \text{B}(\text{C}_6\text{F}_5)_3 \quad \text{N} \quad \text{CH}_2\text{Cl}_2 
\]

4-Acetamidylphenylacetonitrile (0.071 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.19 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield 4-Ethylaminophenylacetonitrile (0.060 g, 92%).

\[\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.10 (d, J = 8.6 \text{ Hz}, 2\text{H}), 6.58 (d, J = 8.6 \text{ Hz}, 2\text{H}), 3.63 (s, 3\text{H}), 3.15 (q, J = 7.1 \text{ Hz}, 2\text{H}), 1.26 (t, J = 7.1 \text{ Hz}, 3\text{H}).\]

\[\text{13C NMR (101 MHz, CDCl}_3\text{)} \delta 148.13, 128.89, 118.69, 117.76, 113.02, 38.43, 22.81, 14.79. \text{HRMS (ESI) } m/z 161.1072 \text{ [calc’d for } \text{C}_{10}\text{H}_{12}\text{N}_2 (\text{M}+\text{H}^+) \text{ 161.1073}.}\]

Acetoacetanilide Triethylsilylether (Mixture of E/Z Amide Conformations)

\[
\text{NH} \quad \text{Et}_3\text{SiH} \quad \text{B}(\text{C}_6\text{F}_5)_3 \quad \text{CH}_2\text{Cl}_2 
\]

Acetoacetanilide (0.072 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.20 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield acetoacetanilide triethylsilylether (0.118 g, 89%).

\[\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 8.71 (s, 0.4\text{H}), 8.38 (s, 0.6\text{H}), 7.53 – 7.45 (m, 2\text{H}), 7.35 – 7.24 (m, 2\text{H}), 7.16 – 7.03 (m, 1\text{H}), 4.34 – 4.16 (m, 1\text{H}), 2.69 – 2.31 (m, 2\text{H}), 1.29 (d, J = 6.3 \text{ Hz}, 1.2\text{H}), 1.24 (d, J = 6.3 \text{ Hz}, 1.8\text{H}), 0.98 (t, J =
7.9 Hz, 3.6H), 0.93 (t, J = 7.9 Hz, 2.4H), 0.66 (q, J = 7.9 Hz, 2.4H), 0.52 (q, J = 7.9 Hz, 1.6H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 170.9, 170.0, 137.9, 137.6, 129.0, 128.96, 124.5, 124.2, 120.2, 119.8, 66.0, 65.0, 46.6, 44.9, 23.0, 23.0, 6.8, 6.4, 4.8, 4.8. HRMS (ESI) \(m/z\) 294.1880 [calc'd for C\(_{16}\)H\(_{27}\)NO\(_2\)Si (M+H\(^+\)) 294.1884]

**Acetoacetanilide Triethylsilylether (Mixture of E/Z Amide Conformations)**

Acetoacetanilide (0.072 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.20 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield acetoacetanilide triethylsilylether (0.118 g, 89%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.71 (s, 0.4H), 8.38 (s, 0.6H), 7.53 – 7.45 (m, 2H), 7.35 – 7.24 (m, 2H), 7.16 – 7.03 (m, 1H), 4.34 – 4.16 (m, 1H), 2.69 – 2.31 (m, 2H), 1.29 (d, J = 6.3 Hz, 1.2H), 1.24 (d, J = 6.3 Hz, 1.8H), 0.98 (t, J = 7.9 Hz, 3.6H), 0.93 (t, J = 7.9 Hz, 2.4H), 0.66 (q, J = 7.9 Hz, 2.4H), 0.52 (q, J = 7.9 Hz, 1.6H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 170.9, 170.0, 137.9, 137.6, 129.0, 128.96, 124.5, 124.2, 120.2, 119.8, 66.0, 65.0, 46.6, 44.9, 23.0, 23.0, 6.8, 6.4, 4.8, 4.8. HRMS (ESI) \(m/z\) 294.1880 [calc’d for C\(_{16}\)H\(_{27}\)NO\(_2\)Si (M+H\(^+\)) 294.1884]

**p-Chloro-Acetoacetanilide Triethylsilylether**

\(p\)-Chloroacetoacetanilide (0.086 g, 0.409 mmol) was dissolved in dichloromethane (4.1 mL) in a scintillation vial. Triethylsilane (0.20 mL, 1.227 mmol) was then added followed by tris(pentafluorophenyl)borane (0.021 g, 0.0409 mmol). The reaction was allowed to stir for 8 hours before being concentrated under reduced pressure and purified by flash chromatography to yield \(p\)-chloroacetanilide triethylsilylether (0.120 g, 90%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.61 (bs, 1H), 7.46 (d, J = 8.8 Hz, 2H), 7.27 (d, J = 8.8 Hz, 2H), 4.35 – 4.23 (m, 1H), 2.65 (dd, J = 14.9, 3.8 Hz, 1H), 2.40 (dd, J = 14.9, 5.6 Hz, 1H), 1.30 (d, J = 6.3 Hz, 3H), 0.98 (t, J = 7.9 Hz, 8H), 0.66 (q, J = 7.9 Hz, 6H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 169.6, 136.7, 129.0, 128.8, 120.8, 66.0, 65.0, 46.7, 23.0, 6.8, 4.8 HRMS (ESI) \(m/z\) 328.1490 [calc’d for C\(_{16}\)H\(_{26}\)NO\(_2\)ClSi (M+H\(^+\)) 328.1494]
3. $^1$H-NMR and $^{13}$C-NMR Spectra