Supporting Information

Copper-Catalyzed Nucleophilic Trifluoromethylation of Benzylic Chlorides

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General Methods.

\(^1\)H NMR (270 MHz) and \(^{13}\)C NMR (67.8 MHz) spectra were measured on a JEOL Excalibur 270 spectrometer using CDCl\(_3\) as solvent. \(^{19}\)F NMR (471 MHz) spectra were recorded on a JEOL JNM-ECP 500 spectrometer. Elemental analyses were performed at Microanalytical Center of The University of Tokyo. Mass spectra were measured on a JEOL JMS-700 mass spectrometer. Specific rotations were measured on a JASCO DIP-1000 polarimeter.

All reactions were carried out under dry nitrogen atmosphere. Solvents were dried by the usual methods, then distilled under N\(_2\) and degassed before use. CF\(_3\)SiMe\(_3\) is commercially available and was distilled before use. Potassium fluoride (KF) was dried under vacuum at 190 °C overnight and stored in a glove box. Copper (I) thiophene-2-carboxylate (CuTC) was prepared according to the reported method.S\(^1\) Benzylic chlorides 1\(a\) and 1\(b\) were commercially available. Trifluoromethylated product 2\(a\)S\(^2\) was a known compound. Benzylic chlorides 1\(c\),S\(^3\) 1\(e\),S\(^4\) 1\(g\),S\(^5\) 1\(h\),S\(^5\) 1\(j\),S\(^6\) and 1\(k\)S\(^7\) were prepared by the reaction of corresponding alcohols with SOCl\(_2\). Benzylic chlorides 1\(d\),S\(^8\) 1\(f\),S\(^9\) and 1\(i\)S\(^10\) were prepared from corresponding alcohols by the reported methods. \((R)-1\)\(i\) was prepared by the reaction of the corresponding (S)-alcohol (96% ee) with POCl\(_3\) and pyridine.S\(^{11}\)

![Image](image.png)

\(1f\):S\(^9\) A white solid. \(^1\)H NMR \(\delta 7.96-7.99 (m, 1H), 7.76-7.79 (m, 2H), 7.61-7.65 (m, 2H), 7.22-7.38 (m, 4H), 4.73 (s, 2H), 2.35 (s, 3H). \(^{13}\)C NMR \(\delta 145.2, 135.3, 135.1, 130.0, 129.0, 126.9, 125.2, 125.0, 123.4, 119.7, 118.8, 113.7, 37.3, 21.6.

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1g: A white solid. $^1$H NMR $\delta$ 7.74-7.86 (m, 4H), 7.60 (s, 1H), 7.44 (dd, $J = 8.8$ and 1.9 Hz, 1H), 7.24-7.27 (m, 2H), 4.68 (s, 2H), 2.36 (s, 3H). $^{13}$C NMR $\delta$ 145.6, 134.8, 134.0, 130.7, 130.1, 128.2, 126.9, 126.1, 122.6, 118.2, 117.1, 115.2, 36.9, 21.6.

1h: A white solid. $^1$H NMR $\delta$ 7.86 (d, $J = 9.2$ Hz, 1H), 7.74 (d, $J = 8.1$ Hz, 2H), 7.56 (s, 1H), 7.21-7.26 (m, 2H), 6.94-7.04 (m, 2H), 4.70 (s, 2H), 3.84 (s, 3H), 2.34 (s, 3H). $^{13}$C NMR $\delta$ 156.5, 145.1, 135.0, 130.0, 129.9, 126.8, 125.7, 118.7, 114.7, 114.4, 102.0, 55.7, 37.4, 21.5.

**Copper-Catalyzed Trifluoromethylation of Benzylic Chlorides (1)**

A typical experimental procedure for the reaction of $p$-methoxybenzyl chloride (1a) with CF$_3$SiMe$_3$ is described below. In a 20 mL Schlenk flask were placed CuTC (4.7 mg, 0.025 mmol) and KF (87.1 mg, 1.5 mmol). Anhydrous and degassed THF (3.0 mL) was added, and then the mixture was magnetically stirred at room temperature. After the addition of 1a (78.8 mg, 0.50 mmol) and CF$_3$SiMe$_3$ (220 $\mu$L, 1.5 mmol), the reaction flask was kept at 60 °C for 48 h. The solution was poured into water (5 mL) and the resulting mixture was extracted with diethyl ether (30 mL x 3). The combined extracts were washed with brine, and dried over anhydrous MgSO$_4$. After the concentration under reduced pressure, the resulting residue was purified by column chromatography (SiO$_2$, eluent: hexane /AcOEt = 90 / 10) to give 2a as a yellow oil (80.9 mg, 0.425 mmol, 85% isolated yield).$^{52}$

Isolated yields and spectroscopic data of other products are as follows.

2c: 94% Yield. A colorless oil. $^1$H NMR $\delta$ 6.72-6.80 (m, 3H), 5.97 (s, 2H), 3.27 (q, $J = 11.2$ Hz, 2H) $^{13}$C NMR $\delta$ 147.9, 147.5, 125.7 (q, $^1$J$_{C-F} = 276$ Hz), 123.6, 123.5 (q, $^3$J$_{C-F} = 3.3$ Hz), 110.3, 108.4, 101.2, 39.9 (q, $^2$J$_{C-F} = 29.9$ Hz). $^{19}$F NMR $\delta$ -69.0 (t, $J = 11.2$ Hz). HRMS (EI) Calcd for C$_9$H$_7$F$_3$O$_2$
[M]: 204.0398. Found: 204.0400.

2d: 93% Yield. A white solid, m.p. 37.8-39.1 °C. $^1$H NMR δ 8.33 (d, J = 7.0 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.48-7.92 (m, 2H), 7.38 (d, J = 8.3 Hz, 1H), 6.80 (d, J = 8.3 Hz, 1H), 4.01 (s, 3H), 3.77 (q, $J_{CF} = 11.1$ Hz, 2H). $^{13}$C NMR δ 155.8, 133.1, 129.5, 127.0, 126.2 (q, $J_{CF} = 277$ Hz), 125.9, 125.2, 123.4 (q, $J_{CF} = 1.1$ Hz), 122.7, 118.3 (q, $J_{CF} = 2.8$ Hz), 103.2, 55.5, 36.4 (q, $J_{CF} = 30.1$ Hz). $^{19}$F NMR δ -67.7 (t, J = 11.1 Hz). HRMS (EI) Calcd for C$_{13}$H$_{11}$F$_3$O [M]: 240.0762. Found: 240.0760.

2e: 82% NMR yield. A colorless oil. $^1$H NMR δ 7.29 (dd, J = 1.8 and 4.7 Hz, 1H), 6.99-7.02 (m, 2H), 3.60 (q, $J_{CF} = 11.0$ Hz, 2H). $^{13}$C NMR δ 130.6 (q, $J_{CF} = 3.3$ Hz), 128.7, 127.1, 126.0, 125.0 (q, $J_{CF} = 276$ Hz), 34.6 (q, $J_{CF} = 32.2$ Hz). $^{19}$F NMR δ -69.4 (t, J = 11.0 Hz). HRMS (EI) Calcd for C$_6$H$_5$F$_3$S [M]: 166.0064. Found: 166.0066.

2f: 86% Yield. A white solid, m.p. 123.7-125.2 °C. $^1$H NMR δ 7.98 (d, J = 7.6 Hz, 1H), 7.76 (d, J = 8.4 Hz, 2H), 7.58 (s, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.21-7.37 (m, 4H), 3.47 (q, J = 11.0 Hz, 2H), 2.34 (s, 3H). $^{13}$C NMR δ 145.5, 134.7, 133.6, 131.9, 129.9, 126.7, 126.0, 125.6 (q, $J_{CF} = 276.4$ Hz), 125.0, 123.4, 119.3 (q, $J_{CF} = 1.1$ Hz), 113.6, 111.3 (q, $J_{CF} = 3.3$ Hz), 30.2 (q, $J_{CF} = 31.8$ Hz), 21.4. $^{19}$F NMR δ -68.2 (t, J = 11.0 Hz). Anal. Calcd for C$_{17}$H$_{14}$F$_3$NO$_2$S: C, 57.78; H, 3.99; N, 3.96. Found: C, 57.45; H, 4.10; N, 3.83.

2g: 90% Yield. A white solid, m.p. 151.3-153.2 °C. $^1$H NMR δ 7.85 (d, J = 8.8 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.58-7.62 (m, 2H), 7.43 (dd, J = 8.8 and 1.8 Hz, 1H), 7.23 (d, J = 8.4 Hz, 2H), 3.42 (q, J = 11.0 Hz, 2H), 2.34 (s, 3H). $^{13}$C NMR δ 145.5, 134.7, 133.6, 131.9, 130.1, 128.0, 127.2, 126.8,
125.6 (q, $^1J_{C-F} = 276.4$ Hz), 122.2, 117.1, 115.1, 110.7 (q, $^3J_{C-F} = 3.3$ Hz), 30.3 (q, $^2J_{C-F} = 32.0$ Hz), 21.6. $^{19}$F NMR $\delta$ -68.2 (t, $J = 11.0$ Hz). Anal. Calcd for C$_{17}$H$_{13}$BrF$_3$NO$_2$S: C, 47.24; H, 3.03; N, 3.24. Found: C, 47.15; H, 3.18; N, 3.23.

$^2$h: 89% Yield. A white solid, m. p. 124.7-126.5°C. $^1$H NMR $\delta$ 7.87 (d, $J = 9.2$ Hz, 1H), 7.72 (d, $J = 8.4$ Hz, 2H), 7.53 (s, 1H), 7.20-7.26 (m, 2H), 6.90-6.97 (m, 2H), 3.82 (s, 3H), 3.43 (q, $^1J_{C-F} = 11.0$ Hz, 2H), 2.34 (s, 3H). $^{13}$C NMR $\delta$ 156.6, 145.0, 135.0, 131.2, 129.9, 129.6, 126.8, 126.7, 125.6 (q, $^1J_{C-F} = 276.3$ Hz), 114.6, 114.1, 111.4 (q, $^3J_{C-F} = 3.2$ Hz), 101.7, 55.6, 30.4 (q, $^2J_{C-F} = 32.0$ Hz), 21.5. $^{19}$F NMR $\delta$ -68.1 (t, $J = 11.0$ Hz). Anal. Calcd for C$_{18}$H$_{16}$F$_3$NO$_3$S: C, 56.39; H, 4.21; N, 3.65. Found: C, 56.29; H, 4.34; N, 3.38.

$^2$i: 75% Yield. A colorless oil. $^1$H NMR $\delta$ 7.21 (d, $J = 8.4$ Hz, 2H), 7.16 (d, $J = 8.4$ Hz, 2H), 3.32-3.48 (m, 1H), 2.35 (s, 3H), 1.49 (d, $J = 7.3$ Hz, 3H). $^{13}$C NMR $\delta$ 137.8, 133.4 (q, $^3J_{C-F} = 1.9$ Hz), 129.3, 128.3, 127.2 (q, $^1J_{C-F} = 278.8$ Hz), 43.8 (q, $^2J_{C-F} = 27.5$ Hz), 21.0, 14.6 (q, $^3J_{C-F} = 2.8$ Hz). $^{19}$F NMR $\delta$ -74.2 (d, $J = 11.3$ Hz). HRMS (EI) Calcd for C$_{10}$H$_{11}$F$_3$ [M]: 188.0813. Found: 188.0806.

$^2$j: 42% Yield. A colorless oil. $^1$H NMR $\delta$ 7.16 (br, 4H), 3.00-3.16 (m, 1H), 2.35 (s, 3H), 1.98-2.13 (m, 1H), 1.76-1.93 (m, 1H), 0.83 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR $\delta$ 137.7, 131.7 (q, $^3J_{C-F} = 2.2$ Hz), 129.3, 128.9, 127.1 (q, $^1J_{C-F} = 279.3$ Hz), 51.4 (q, $^2J_{C-F} = 26.2$ Hz), 22.0 (q, $^3J_{C-F} = 2.3$ Hz), 21.1, 11.5. $^{19}$F NMR $\delta$ -72.5 (d, $J = 11.3$ Hz). HRMS (EI) Calcd for C$_{11}$H$_{13}$F$_3$ [M]: 202.0969. Found: 202.0963.

Copper-Catalyzed Trifluoromethylation of (R)-1i
In a 20 mL Schlenk flask were placed CuTC (4.8 mg, 0.025 mmol) and KF (87.4 mg, 1.5 mmol). Anhydrous and degassed THF (3.0 mL) was added, and then the mixture was magnetically stirred at room temperature. After the addition of (R)-1i (77.4 mg, 0.50 mmol, 60% ee) and CF₃SiMe₃ (220 µL, 1.5 mmol), the reaction flask was kept at 60 °C for 48 h. The solution was poured into water (5 mL) and the resulting mixture was extracted with diethyl ether (30 mL x 3). The combined extracts were washed with brine, and dried over anhydrous MgSO₄. After the concentration under reduced pressure, the resulting residue was purified by column chromatography (SiO₂, eluent: hexane only) to give 2i as a colorless oil (61.7 mg, 0.328 mmol, 66% isolated yield). [α]²⁵_D = −0.4 (c = 0.705, CHCl₃).

References and Notes
(S2) Riss, P. J.; Aigbirhio, F. I. Chem. Commun. 2011, 47, 11873.