Copper(II)-Catalyzed Trifluoromethylation of N-Aryl Imines

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A. General Information

General Procedures. All reactions were performed in oven-dried or flame-dried round-bottom flasks and vials. Stainless steel syringes and cannula were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed using silica gel 60 (230-400 mesh) from Sigma Aldrich.

Materials. Commercial reagents were purchased from Sigma Aldrich, Fluka, EM Science, and Lancaster and used as received. All solvents were used after being freshly distilled unless otherwise noted.

Instrumentation. Proton nuclear magnetic resonance ($^1$H NMR) spectra and carbon nuclear magnetic resonance ($^{13}$C NMR) spectra were recorded on Bruker UltraShield-400 (400 MHz). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to the NMR solvent residual peak (CHCl$_3$: $\delta$ 7.26). Chemical shifts for carbons are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the NMR solvent (CDCl$_3$: $\delta$ 77.0). For those complicated spin-spin splitting patterns, coupling constants were obtained by 2D J-resolve experiments. Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), coupling constants in Hertz (Hz), and integration.

The mass spectroscopic data were obtained at the Georgia State University mass spectrometry facility using a Micromass Platform II single quadrupole instrument. Infrared (IR) spectra were obtained by using a Perkin Elmer Spectrum 100 FT-IR spectrometer. Data are represented as follows: frequency of absorption (cm$^{-1}$).

B. Catalyst Discovery for Copper(II)-Catalyzed Trifluoromethylation of N-Aryl Imines

Table S1. Catalyst Discovery for Trifluoromethylation of N-Aryl Imines

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>additive (equiv)</th>
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<tr>
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<td>KF (3.0)</td>
<td>&lt;5%</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>CuI</td>
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<td>&lt;5%</td>
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<tr>
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<td>CuBr₂</td>
<td>KF (3.0)</td>
<td>&lt;5%</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>CuOAc</td>
<td>KF (3.0)</td>
<td>35%</td>
<td>23%</td>
</tr>
<tr>
<td>5</td>
<td>Cu(OAc)₂</td>
<td>KF (3.0)</td>
<td>&gt;95%</td>
<td>65%</td>
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<tr>
<td>6</td>
<td>Cu(TFA)₂</td>
<td>KF (3.0)</td>
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<td>24%</td>
</tr>
<tr>
<td>7</td>
<td>Cu(OTf)₂</td>
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<tr>
<td>8</td>
<td>CuSO₄</td>
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<tr>
<td>9</td>
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<td>LiOAc (1.0)</td>
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</tr>
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Table S2. Temperature and TMSCF₃ Quantity Screen

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<th>yield</th>
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</tr>
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<td>2</td>
<td>40 °C</td>
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<td>81%</td>
</tr>
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General Procedure

To a flame-dried sealable 2-dram vial equipped with a stir bar were added 43.2 mg of 8-aminoquinoline (0.3 mmol, 1.0 equiv), 37 µL of freshly distilled benzaldehyde (0.36 mmol, 1.2 equiv), 0.1 g of freshly activated molecular sieves (4 Å) and 2 mL of toluene and the mixture was stirred for 1 h at room temperature to afford the imine (note: the progress of imine formation was monitored by ¹H NMR in CDCl₃ (pretreated with K₂CO₃). The solution was then added to a vial that was charged with copper salts (0.06 mmol, 20 mol %) and additives (not in the case of entry
10) under argon. The mixture was stirred at room temperature for 10 minutes, and 88 µL TMSCF₃ (0.6 mmol, 2.0 equiv) was added. The reaction was warmed to 40 °C for 4 h and quenched with saturated aqueous NaHCO₃ solution. The mixture was first filtered through a short pad of celite (to remove the molecular sieves) and then extracted with EtOAc. The organic phase was concentrated and the crude product was purified by flash column chromatography.

C. Procedure for Cu(OAc)₂-Catalyzed N-Aryl Imine Trifluoromethylation

Table S3. Cu(OAc)₂-Catalyzed N-Aryl Imine Trifluoromethylation

<table>
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<th>entry</th>
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<th>product</th>
<th>yield</th>
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</thead>
<tbody>
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<td>1</td>
<td>phenyl</td>
<td>2</td>
<td>81%</td>
</tr>
<tr>
<td>2</td>
<td>3-Cl-phenyl</td>
<td>S1a</td>
<td>70%</td>
</tr>
<tr>
<td>3</td>
<td>4-F-phenyl</td>
<td>S2a</td>
<td>71%</td>
</tr>
<tr>
<td>4</td>
<td>4-Cl-phenyl</td>
<td>S3a</td>
<td>78%</td>
</tr>
<tr>
<td>5</td>
<td>4-NO₂-phenyl</td>
<td>S4a</td>
<td>72%</td>
</tr>
<tr>
<td>6</td>
<td>4-Br-phenyl</td>
<td>S5a</td>
<td>71%</td>
</tr>
<tr>
<td>7</td>
<td>4-Me-phenyl</td>
<td>S6a</td>
<td>67%</td>
</tr>
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<td>4-MeO-phenyl</td>
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</tr>
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<td>3,4-(Me)₂-phenyl</td>
<td>S8a</td>
<td>63%</td>
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<td>10</td>
<td>2-furyl</td>
<td>S9a</td>
<td>61%</td>
</tr>
<tr>
<td>11</td>
<td>3-pyridyl</td>
<td>S10a</td>
<td>72%</td>
</tr>
<tr>
<td>12</td>
<td>2-pyridyl</td>
<td>S11a</td>
<td>61%</td>
</tr>
<tr>
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<td>cyclohexyl</td>
<td>S12a</td>
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<tr>
<td>14</td>
<td>iso-butyl</td>
<td>S13a</td>
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<tr>
<td>15</td>
<td>cinnamyl</td>
<td>S14a</td>
<td>53%</td>
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</table>

General Procedure

To a flame-dried sealable 2-dram vial equipped with a stir bar were added 43.2 mg of 8-aminoquinoline (0.3 mmol, 1.0 equiv), 37 µL of freshly distilled aldehyde (0.36 mmol, 1.2 equiv), 0.1 g of freshly activated molecular sieves (4 Å) and 2 mL of toluene and the mixture was stirred for 1–12 h at room temperature to afford the imine (note: the progress of imine formation was monitored by ¹H NMR in CDCl₃ (pretreated with K₂CO₃). The solution was then added to a vial that was charged with Cu(OAc)₂ (0.06 mmol, 10.9 mg, 20 mol %) under argon. The mixture was
stirred at room temperature for 10 minutes, and 88 µL TMSCF₃ (0.6 mmol, 2.0 equiv) was added. The reaction was warmed to 40 °C for 4 h (monitoring by TLC until all the 8-aminoquinoline disappears). Then it was quenched with saturated aqueous NaHCO₃ solution. The mixture was first filtered through a short pad of celite (to remove the molecular sieves) and then extracted with EtOAc. The organic phase was concentrated and the crude product was purified by flash column chromatography.

\[ \text{N-(2,2,2-trifluoro-1-phenylethyl)quinolin-8-amine (2)} \]

\[ ^1H \text{ NMR (400 MHz, CDCl}_3, \text{ ppm)} \delta 8.80 (d, J = 2.8 Hz, 1H), 8.07 (d, J = 8.1 Hz, 1H), 7.59 (d, J = 6.5 Hz, 2H), 7.46-7.35 (m, 4H), 7.31 (t, J = 7.9 Hz, 1H), 7.15 (t, J = 7.1 Hz, 2H), 6.65 (d, J = 7.6 Hz, 1H), 5.17-5.13 (m, 1H). \]

\[ ^13C \text{ NMR (100 MHz, CDCl}_3, \text{ ppm)} \delta 147.47, 142.26, 138.26, 135.99, 133.96, 129.06, 128.83, 128.49, 128.04, 127.26, 125.19 (q, J = 281 Hz), 121.65, 116.00, 106.20, 60.13 (q, J = 30 Hz). \]

\[ ^19F \text{ NMR (377 MHz, CDCl}_3, \text{ ppm): } \delta -73.82 (d, J = 7.2 Hz). \]

\[ \text{IR } \nu_{\text{max}} \text{ (neat)/cm}^{-1}: 3362, 2940, 1594, 1520, 1467, 1204, 1148, 818, 702. \]

\[ \text{HRMS (ESI, m/z): calcd for C}_{17}H_{14}F_{3}N_{2}^+ [M+H^+] : 303.1109; \text{ Found: 301.1114}. \]

\[ \text{S1a} \]

\[ \text{N-(1-(3-chlorophenyl)-2,2,2-trifluoroethyl)quinolin-8-amine (S1a)} \]

\[ ^1H \text{ NMR (400 MHz, CDCl}_3, \text{ ppm)} \delta 8.80 (d, J = 2.0 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.58 (s, 1H), 7.51-7.39 (m, 2H), 7.39-7.24 (m, 3H), 7.14 (dd, J = 13.3 Hz, 7.8 Hz, 2H), 6.58 (d, J = 7.2 Hz, 1H), 5.12-5.09 (m, 1H). \]

\[ ^13C \text{ NMR (100 MHz, CDCl}_3, \text{ ppm)} \delta 147.60, 141.90, 138.21, 136.04, 134.84, 130.12, 129.39, 128.50, 128.28, \]
127.19, 126.23, 124.8 (q, \(J = 281 \text{ Hz}\)), 121.77, 116.37, 106.22, 59.83 (q, \(J = 30 \text{ Hz}\)). \(^{19}\text{F} \text{ NMR} \ (377 \text{ MHz, CDCl}_3, \text{ ppm})\): \(\delta -73.75 \) (d, \(J = 7.1 \text{ Hz}\)). \(\text{IR } \nu_{\text{max}} \) (neat)/cm\(^{-1}\): 3358, 3006, 1578, 1520, 1275, 1260, 1175, 1126, 765, 744. \(\text{HRMS (ESI, m/z): calcd for C}_{17}\text{H}_{13}\text{ClF}_3\text{N}_2^+ \ [\text{M+H}^+] : 337.0719; \text{Found: 337.0724.} \)

\[ \text{N-(2,2,2-trifluoro-1-(4-fluorophenyl)ethyl)quinolin-8-amine (S2a)} : \]

\(^{1}\text{H} \text{ NMR} \ (400 \text{ MHz, CDCl}_3, \text{ ppm})\): \(\delta 8.80 \) (s, 1H), 8.08 (d, \(J = 8.0 \text{ Hz}, 1\text{H}\)), 7.56-7.53 (m, 2H), 7.43-7.41 (m, 1H), 7.29 (t, \(J = 7.7 \text{ Hz}, 1\text{H}\)), 7.16-7.06 (m, 4H), 6.58 (d, \(J = 7.5 \text{ Hz}, 1\text{H}\)), 5.15-5.08 (m, 1H). \(^{13}\text{C} \text{ NMR} \ (100 \text{ MHz, CDCl}_3, \text{ ppm})\): \(\delta 164.37, 161.91, 147.56, 142.07, 138.28, 136.04, 129.85, 129.77, 128.53, 127.21, 124.0 \) (q, \(J = 280 \text{ Hz}\)), 121.74, 116.23, 116.00, 115.78, 106.28, 59.61 (q, \(J = 30 \text{ Hz}\)). \(^{19}\text{F} \text{ NMR} \ (377 \text{ MHz, CDCl}_3, \text{ ppm})\): \(\delta -74.11 \) (d, \(J = 7.1 \text{ Hz}\)), -112.58 (t, \(J = 4.5 \text{ Hz}\)). \(\text{IR } \nu_{\text{max}} \) (neat)/cm\(^{-1}\): 3345, 2989, 1578, 1510, 1275, 1260, 1173, 1124, 768, 743. \(\text{HRMS (ESI, m/z): calcd for C}_{17}\text{H}_{13}\text{F}_4\text{N}_2^+ \ [\text{M+H}^+] : 321.1051; \text{Found: 321.1013.} \)

\[ \text{N-(1-(4-chlorophenyl)-2,2,2-trifluoroethyl)quinolin-8-amine (S3a)} : \]

\(^{1}\text{H} \text{ NMR} \ (400 \text{ MHz, CDCl}_3, \text{ ppm})\): \(\delta 8.79 \) (d, \(J = 3.2 \text{ Hz}, 1\text{H}\)), 8.08 (d, \(J = 8.0 \text{ Hz}, 1\text{H}\)), 7.51 (d, \(J = 8.4 \text{ Hz}, 2\text{H}\)), 7.42 (dd, \(J = 8.2 \text{ Hz}, 4.2 \text{ Hz}, 1\text{H}\)), 7.37 (d, \(J = 8.4 \text{ Hz}, 2\text{H}\)), 7.29 (t, \(J = 8.0 \text{ Hz}, 1\text{H}\)), 7.15 (d, \(J = 8.4 \text{ Hz}, 1\text{H}\)), 7.12 (d, \(J = 7.6 \text{ Hz}, 1\text{H}\)), 6.57 (d, \(J = 7.6 \text{ Hz}, 1\text{H}\)), 5.13-5.08 (m, 1H). \(^{13}\text{C} \text{ NMR} \ (100 \text{ MHz, CDCl}_3, \text{ ppm})\): \(\delta 147.58, 141.93, 138.23, 136.06, 135.11, 132.48, 129.41, 129.10, 128.50, 127.18, 124.9 \) (q, \(J = 280 \text{ Hz}\)), 121.76, 116.32, 106.30, 59.68 (q, \(J = 30.0 \text{ Hz}\)). \(^{19}\text{F} \text{ NMR} \ (377 \text{ MHz, CDCl}_3, \text{ ppm})\): \(\delta -73.95 \) (d,
\( J = 7.1 \text{ Hz} \). IR \( \nu_{\text{max}} \) (neat)/cm\(^{-1}\): 3356, 2892, 1521, 1172, 1126, 817, 764, 748. HRMS (ESI, m/z): calcd for C\(_{17}\)H\(_{13}\)ClF\(_3\)N\(_2\) \([\text{M+H}^+]\): 337.0719; Found: 337.0715.

![Image of S4a](image)

**N-(2,2,2-trifluoro-1-(4-nitrophenyl)ethyl)quinolin-8-amine (S4a)**: \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \( \delta \) 8.77 (d, \( J = 2.0 \text{ Hz} \), 1H), 8.21 (d, \( J = 8.8 \text{ Hz} \), 2H), 8.06 (d, \( J = 7.6 \text{ Hz} \), 1H), 7.73 (d, \( J = 8.4 \text{ Hz} \), 2H), 7.41 (dd, \( J = 7.9 \text{ Hz} \), 4.0 Hz, 1H), 7.24 (d, \( J = 8.0 \text{ Hz} \), 1H), 7.15 (t, \( J = 8.4 \text{ Hz} \), 2H), 6.47 (d, \( J = 7.2 \text{ Hz} \), 1H), 5.23-5.18 (m, 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\), ppm) \( \delta \) 147.78, 141.50, 141.09, 138.20, 136.13, 129.19, 128.53, 127.07, 124.5 (q, \( J = 280 \text{ Hz} \)), 124.03, 121.93, 116.85, 106.35, 59.89 (q, \( J = 31 \text{ Hz} \)). \(^{19}\)F NMR (377 MHz, CDCl\(_3\), ppm) \( \delta \) -73.48 (d, \( J = 6.8 \text{ Hz} \)). IR \( \nu_{\text{max}} \) (neat)/cm\(^{-1}\): 3362, 2990, 1578, 1479, 1275, 1260, 1127, 767, 745. HRMS (ESI, m/z): calcd for C\(_{17}\)H\(_{13}\)F\(_3\)N\(_3\)O\(_2\) \([\text{M+H}^+]\): 348.0960; Found: 348.0955.

![Image of S5a](image)

**N-(1-(4-bromophenyl)-2,2,2-trifluoroethyl)quinolin-8-amine (S5a)**: \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \( \delta \) 8.79 (d, \( J = 2.8 \text{ Hz} \), 1H), 8.08 (d, \( J = 8.4 \text{ Hz} \), 1H), 7.52 (d, \( J = 8.0 \text{ Hz} \), 2H), 7.46-7.40 (m, 3H), 7.29 (t, \( J = 8.0 \text{ Hz} \), 1H), 7.13 (dd, \( J = 15.6 \text{ Hz} \), 7.8 Hz, 2H), 6.57 (d, \( J = 7.6 \text{ Hz} \), 1H), 5.13-5.06 (m, 1H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\), ppm) \( \delta \) 147.58, 141.93, 138.24, 136.05, 133.02, 132.06, 129.72, 128.50, 127.18, 124.8 (q, \( J = 280 \text{ Hz} \)), 123.29, 121.76, 116.34, 106.31, 59.77 (q, \( J = 30 \text{ Hz} \)). \(^{19}\)F NMR (377 MHz, CDCl\(_3\), ppm) \( \delta \) -73.92 (d, \( J = 7.0 \text{ Hz} \)). IR \( \nu_{\text{max}} \) (neat)/cm\(^{-1}\): 3351, 3005, 1520, 1479, 1275, 1260, 1126, 756, 743. HRMS (ESI, m/z): calcd for C\(_{17}\)H\(_{13}\)BrF\(_3\)N\(_2\) \([\text{M+H}^+]\): 381.0214; Found: 381.0216.
**N-(2,2,2-trifluoro-1-p-tolylethyl)quinolin-8-amine (S6a)**: $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.78 (d, $J = 3.2$ Hz, 1H), 8.07 (d, $J = 8.0$ Hz, 1H), 7.45 (d, $J = 8.0$ Hz, 2H), 7.40 (dd, $J = 8.2$ Hz, 4.2 Hz, 1H), 7.30 (t, $J = 8.0$ Hz, 1H), 7.20 (d, $J = 8.0$ Hz, 2H), 7.14-7.09 (m, 2H), 6.64 (d, $J = 7.6$ Hz, 1H), 5.11-5.07 (m, 1H), 2.35 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 147.43, 142.34, 138.95, 138.27, 135.98, 130.95, 129.53, 128.49, 127.90, 127.28, 125.2 (q, $J = 280$ Hz), 121.63, 115.90, 106.19, 59.74 (q, $J = 30.0$ Hz), 21.16. $^{19}$F NMR (377 MHz, CDCl$_3$, ppm) $\delta$ -73.96 (d, $J = 7.2$ Hz). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3335, 2923, 1578, 1521, 1253, 1170, 1124, 818, 790. HRMS (ESI, m/z): calcd for C$_{18}$H$_{16}$F$_3$N$_2^{+}$ [M+H$^+$]: 317.1266; Found: 317.1267.

**N-(2,2,2-trifluoro-1-(4-methoxyphenyl)ethyl)quinolin-8-amine (S7a)**: $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.78 (d, $J = 2.8$ Hz, 1H), 8.07 (d, $J = 8.4$ Hz, 1H), 7.48 (d, $J = 8.0$ Hz, 2H), 7.40 (dd, $J = 8.1$ Hz, 4.1 Hz, 1H), 7.30 (t, $J = 7.6$ Hz, 1H), 7.13 (d, $J = 8.0$ Hz, 1H), 7.08 (d, $J = 7.2$ Hz, 1H), 6.92 (d, $J = 8.8$ Hz, 2H), 6.64 (d, $J = 7.2$ Hz, 1H), 5.11-5.04 (m, 1H), 3.80 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 160.12, 147.44, 142.35, 138.29, 135.99, 129.20, 128.50, 128.50, 127.28, 125.91, 125.2 (q, $J = 280$ Hz), 121.63, 115.91, 114.25, 106.25, 59.61 (q, $J = 30$ Hz), 55.25. $^{19}$F NMR (377 MHz, CDCl$_3$, ppm) $\delta$ -74.15 (d, $J = 7.1$ Hz). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3339, 3006, 1614, 1513, 1275, 1260, 1123, 760, 741. HRMS (ESI, m/z): calcd for C$_{18}$H$_{16}$F$_3$N$_2$O$^-$ [M+H$^-$]: 333.1215; Found: 333.1216.
**N-(1-(3,4-dimethylphenyl)-2,2,2-trifluoroethyl)quinolin-8-amine (S8a):**  
$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.79-8.78 (m, 1H), 8.07 (d, $J$ = 8.4 Hz, 1H), 7.40 (dd, $J$ = 8.2 Hz, 4.2 Hz, 1H), 7.32-7.28 (m, 3H), 7.14 (t, $J$ = 9.6 Hz, 2H), 7.07 (d, $J$ = 7.2 Hz, 1H), 6.67 (d, $J$ = 7.6 Hz, 1H), 5.07-5.02 (m, 1H), 2.27 (s, 3H), 2.25 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 147.42, 142.50, 138.31, 137.64, 137.14, 135.99, 131.39, 130.07, 129.18, 128.52, 127.34, 125.39, 125.3 (q, $J$ = 280 Hz), 121.63, 115.84, 106.16, 59.96 (q, $J$ = 31 Hz), 19.86, 19.52. $^{19}$F NMR (377 MHz, CDCl$_3$, ppm) $\delta$ -73.87 (d, $J$ = 7.2 Hz). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3341, 2989, 1578, 1520, 1275, 1260, 1123, 763, 751. HRMS (ESI, m/z): calcd for C$_{19}$H$_{18}$F$_3$N$_2$ $^+ [M+H]$: 331.1422; Found: 331.1410.

**N-(2,2,2-trifluoro-1-(furan-2-yl)ethyl)quinolin-8-amine (S9a):**  
$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.78 (d, $J$ = 3.2 Hz, 1H), 8.08 (d, $J$ = 8.0 Hz, 1H), 7.47 (s, 1H), 7.46-7.38 (m, 2H), 7.19 (d, $J$ = 8.0 Hz, 1H), 7.01 (d, $J$ = 8.8 Hz, 1H), 6.84 (d, $J$ = 7.6 Hz, 1H), 6.55 (d, $J$ = 3.2 Hz, 1H), 6.40 (s, 1H), 5.36-5.29 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 147.55, 143.33, 142.22, 138.29, 136.00, 128.59, 127.24, 124.50 (q, $J$ = 281 Hz), 121.68, 116.42, 110.62, 109.49, 106.02, 54.46 (q, $J$ = 32 Hz). $^{19}$F NMR (377 MHz, CDCl$_3$, ppm) $\delta$ -74.27 (d, $J$ = 6.6 Hz). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3348, 2989, 1579, 1520, 1280, 1275, 1151, 770, 759. HRMS (ESI, m/z): calcd for C$_{15}$H$_{12}$F$_3$N$_2$ $^+ [M+H]$: 293.0902; Found: 293.0906.
**N-(2,2,2-trifluoro-1-(pyridin-3-yl)ethyl)quinolin-8-amine (S10a):**

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 8.81-8.79 (m, 2H), 8.63 (s, 1H), 8.07 (d, $J = 8.0$ Hz, 1H), 7.91 (d, $J = 7.6$ Hz, 1H), 7.42 (dd, $J = 7.8$ Hz, 3.9 Hz, 1H), 7.32-7.26 (m, 2H), 7.17-7.13 (m, 2H), 6.61 (d, $J = 7.2$ Hz, 1H), 5.21-5.18 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) δ 150.50, 149.81, 147.67, 141.74, 138.27, 136.08, 135.31, 129.97, 128.55, 127.17, 124.8 (q, $J = 280$ Hz), 123.80, 121.83, 116.63, 106.37, 58.31 (q, $J = 31$ Hz). $^{19}$F NMR (377 MHz, CDCl$_3$, ppm) δ -73.90 (d, $J = 6.9$ Hz). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3341, 3006, 1579, 1521, 1275, 1260, 1127, 756, 741. HRMS (ESI, m/z): calcd for C$_{16}$H$_{13}$F$_3$N$_3$ $^+$ [M+H$^+$]: 304.1062; Found: 304.1051.

**N-(2,2,2-trifluoro-1-(pyridin-2-yl)ethyl)quinolin-8-amine (S11a):**

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 8.82 (s, 1H), 8.73 (d, $J = 2.0$ Hz, 1H), 8.06 (d, $J = 8.0$ Hz, 1H), 7.76 (d, $J = 7.2$ Hz, 1H), 7.70 (t, $J = 7.6$ Hz, 1H), 7.53 (d, $J = 7.6$ Hz, 1H), 7.41-7.29 (m, 3H), 7.15 (d, $J = 8.0$ Hz, 1H), 6.81 (d, $J = 7.2$ Hz, 1H), 5.33-5.29 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) δ 153.06, 149.70, 147.58, 142.66, 138.44, 136.85, 135.92, 128.62, 127.30, 125.2 (q, $J = 282$ Hz), 123.85, 123.06, 121.62, 116.01, 106.17, 60.74 (q, $J = 30$ Hz). $^{19}$F NMR (377 MHz, CDCl$_3$, ppm) δ -73.28 (d, $J = 6.7$ Hz). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3363, 3006, 1579, 1514, 1275, 1260, 1121, 765, 746. HRMS (ESI, m/z): calcd for C$_{16}$H$_{13}$F$_3$N$_3$ $^+$ [M+H$^+$]: 304.1062; Found: 304.1065.
**N-(1-cyclohexyl-2,2,2-trifluoroethyl)quinolin-8-amine** (S12a): ¹H NMR (400 MHz, CDCl₃, ppm) δ 8.78 (dd, J = 4.4, 2.0 Hz, 1H), 8.10 (d, J = 4.4 Hz, 2.0 Hz, 1H), 7.43-7.28 (m, 2H), 7.14 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 6.80 (d, J = 3.6 Hz, 1H), 6.60 (d, J = 6.0 Hz, 1H), 4.00-3.95 (m, 1H), 2.17-2.02 (m, 2H), 1.84-1.68 (m, 4H), 1.38-1.29 (m, 4H), 1.20-1.17 (m, 1H). ¹³C NMR (100 MHz, CDCl₃, ppm) δ 147.24, 144.01, 138.08, 136.02, 130.68, 128.70, 127.85, 127.47, 125.02, 122.19, 121.57, 115.10, 105.29, 59.72 (q, J = 28 Hz), 38.67, 30.38, 27.44, 26.16, 25.98, 25.92. ¹⁹F NMR (377 MHz, CDCl₃, ppm): δ -71.57 (d, J = 8.0 Hz). IR ν max (neat)/cm⁻¹: 3388, 3006, 1579, 1521, 1275, 1260, 1127, 756, 741. HRMS (ESI, m/z): calcd for C₁₇H₂₀F₃N₂⁺ [M+H⁺]: 309.1579; Found: 309.1569.

**N-(1,1,1-trifluoro-3-methylbutan-2-yl)quinolin-8-amine** (S13a): ¹H NMR (400 MHz, CDCl₃, ppm) δ 8.77 (d, J = 3.2 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.43-7.39 (m, 2H), 7.15 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H), 6.60 (d, J = 9.2 Hz, 1H) 4.03-3.94 (m, 1H), 2.43-2.35 (m, 1H), 1.20 (d, J = 6.8 Hz, 3H), 1.11 (d, J = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, ppm) δ 147.25, 144.04, 138.12, 136.01, 130.67, 128.67, 127.46, 126.43 (q, J = 283 Hz), 121.58, 115.21, 105.43, 59.83 (q, J = 28 Hz), 28.73, 20.34, 17.19. ¹⁹F NMR (377 MHz, CDCl₃, ppm): δ -72.16 (d, J = 7.8 Hz). IR ν max (neat)/cm⁻¹: 3372, 3006, 1579, 1521, 1275, 1260, 1127, 756, 741. HRMS (ESI, m/z): calcd for C₁₄H₁₆F₃N₂⁺ [M+H⁺]: 269.1266; Found: 269.1260.
(E)-N-(1,1,1-trifluoro-4-phenylbut-3-en-2-yl)quinolin-8-amine (S14a): $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.81 (d, $J = 2.0$ Hz, 1H), 8.10 (d, $J = 8.0$ Hz, 1H), 7.46-7.42 (m, 4H), 7.37-7.28 (m, 3H), 7.21 (d, $J = 8.0$ Hz, 1H), 6.92 (d, $J = 16$ Hz, 1H), 6.88 (d, $J = 8.0$ Hz, 1H), 6.78 (d, $J = 8.0$ Hz, 1H), 6.37 (dd, $J = 16$ Hz, 6.4, Hz, 1H), 4.92-4.83 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 147.40, 142.46, 138.20, 136.04, 135.60, 129.58, 128.60, 128.41, 127.34, 126.78, 123.96, 121.65, 120.57, 116.00, 105.94, 57.82 (q, $J = 31$ Hz). $^{19}$F NMR (377 MHz, CDCl$_3$, ppm): $\delta$ -74.85 (d, $J = 6.9$ Hz). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3362, 2940, 1594, 1520, 1467, 1204, 1148, 1067, 818, 702. HRMS (ESI, m/z): calcd for C$_{19}$H$_{16}$F$_3$N$_2$ [M+H$^+$]: 329.1266; Found: 329.1262.

D. Control Experiments for Mechanistic Studies

Scheme S1. Imine Trifluoromethylation with a Picolylamine-Derived Imine

a. Procedure for Imine Trifluoromethylation with a Picolylamine-Derived Imine

To a flame-dried sealable 2-dram vial equipped with a stir bar were added 33 mg of picolylamine (0.3 mmol, 1.0 equiv), 37 µL of freshly distilled benzaldehyde (0.36 mmol, 1.2 equiv), 0.1 g of activated 4 Å molecular sieves and 2 mL of toluene and the mixture was stirred for 1 h at room temperature to afford imines in situ. The imine solution was added to a vial which was charged with 11 mg of Cu(OAc)$_2$ (0.06 mmol, 20 mol%) under argon, and then 88 µL of TMSCF$_3$ (0.6 mmol, 2.0 equiv) was added. The reaction mixture was stirred at 40 ºC for 2 h (monitoring by TLC, until the imine disappears). Then the reaction was quenched with saturated aqueous NaHCO$_3$ solution. The mixture was first filtered through a short pad of celite (to remove the molecular sieves) and then
extracted with EtOAc. The organic phase was concentrated and the crude product was purified by flash column chromatography to afford 4 and 5.

![Image of compound 4]

**2,2,2-Trifluoro-1-phenyl-N-(pyridin-2-ylmethyl)ethanamine (4)**: $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.55 (d, $J = 4.8$ Hz, 1H), 7.63 (t, $J = 7.6$ Hz, 1H), 7.42-7.38 (m, 5H), 7.22-7.16 (m, 2H), 4.19 (q, $J = 7.2$ Hz, 1H), 3.86 (AB, $J = 14.4$ Hz, 2H), 3.13 (br, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 158.36, 149.36, 136.52, 134.02, 129.04, 128.73, 128.68, 126.79, 123.99, 122.35, 122.22, 64.11 (q, $J = 29$ Hz), 52.39. $^{19}$F NMR (377 MHz, CDCl$_3$, ppm): $\delta$ -73.21 (d, $J = 7.4$ Hz). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3383, 2955, 1577, 1521, 1482, 1267, 1194, 1086, 816, 742. HRMS (ESI, m/z): calcd for C$_{14}$H$_{14}$F$_3$N$_2$+[M+H$^+$]: 267.1109; Found: 267.1111.

![Image of compound 5]

**N-benzyl-2,2,2-trifluoro-1-(pyridin-2-yl)ethanamine (5)**: $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.67 (d, $J = 4.4$ Hz, 1H), 7.70 (t, $J = 7.6$ Hz, 1H), 7.34-7.25 (m, 7H), 4.24 (q, $J = 7.2$ Hz, 1H), 3.80 (AB, $J = 13.2$ Hz, 2H), 3.00 (br, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 153.57, 149.58, 138.97, 136.55, 129.26, 128.40, 128.15, 127.21, 126.46, 124.21, 123.64, 63.64 (q, $J = 28$ Hz), 51.46. $^{19}$F NMR (377 MHz, CDCl$_3$, ppm): $\delta$ -73.27 (d, $J = 7.5$ Hz). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3321, 3068, 2931, 2854, 1591, 1263, 1165, 1154, 997, 892, 747, 698. HRMS (ESI, m/z): calcd for C$_{14}$H$_{14}$F$_3$N$_2$+[M+H$^+$]: 267.1109; Found: 267.1113.
Scheme S2. Exploration of Imine Trifluoromethylation with Other Picolylamine-Derived Imines

A series of mono- and di-α-substituted picolylamine derived imines were tested; however, none of them are suitable substrates for imine trifluoromethylation.

Scheme S3. Imine Trifluoromethylation without the quinolinyl directing group

*N-(2,2,2-trifluoro-1-(pyridin-2-yl)ethyl)aniline* (7): $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.68 (d, $J = 4.8$ Hz, 1H), 7.74 (t, $J = 7.6$ Hz, 1H), 7.43 (d, $J = 7.6$ Hz, 1H), 7.34 (t, $J = 6.0$ Hz, 1H), 7.22 (t, $J = 7.6$ Hz, 2H), 6.83-6.79 (m, 3H), 5.60 (d, $J = 7.2$ Hz, 1H), 5.05 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 152.05, 149.42, 146.23, 136.81, 129.34, 125.05 (q, $J = 281$ Hz), 123.95, 123.79, 119.05, 114.12, 60.53 (q, $J = 30$ Hz). $^{19}$F NMR (377 MHz, CDCl$_3$, ppm): $\delta$ -73.87 (d, $J = 37$ Hz). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3402, 1605, 1508, 1434, 1269, 1248, 1167, 999, 749, 693. calcd for C$_{13}$H$_{12}$F$_3$N$_2$ [M+H$^+$]: 253.0953; Found: 253.0951.
4-Methyl-N-(2,2,2-trifluoro-1-phenyl-1-(pyridin-2-yl)ethyl)aniline (9): $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.75 (d, $J$ = 4.4 Hz, 1H), 7.67 (d, $J$ = 6.8 Hz, 2H), 7.61 (t, $J$ = 7.6 Hz, 1H), 7.47-7.43 (m, 3H), 7.33-7.30 (m, 1H), 7.19 (s, 1H), 7.06 (d, $J$ = 8.0 Hz, 1H), 6.90 (d, $J$ = 8.0 Hz, 2H), 6.90 (d, $J$ = 8.0 Hz, 2H), 6.53 (d, $J$ = 8.0 Hz, 2H), 6.25 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 156.47, 147.21, 141.66, 137.79, 136.57, 128.99, 128.77, 128.42, 128.40, 128.16, 127.22, 126.30 (q, $J$ = 290 Hz), 125.03, 123.26, 116.30, 68.79 (q, $J$ = 26 Hz), 20.28. $^{19}$F NMR (377 MHz, CDCl$_3$, ppm): $\delta$ -66.88. IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3346, 1615, 1516, 1257, 1146, 932, 699. HRMS (ESI, m/z): calcd for C$_{20}$H$_{18}$F$_3$N$_2$ [M+H$^+$]: 343.1422; Found: 343.1419.

b. Procedure for Imine Trifluoromethylation in the presence of TEMPO

**Scheme S4.** Imine Trifluoromethylation in the presence of TEMPO

To a flame-dried sealable 2-dram vial equipped with a stir bar were added 8-aminoquinoline (43.2 mg, 0.3 mmol, 1.0 equiv), freshly distilled benzaldehyde (37 µL, 0.36 mmol, 1.2 equiv), activated molecular sieves (4 Å, 0.1 g) and 2 mL toluene and the mixture was stirred for 1 h at room temperature to afford the imine. Without purification, the imine was added to a vial which was charged with Cu(OAc)$_2$ (10.9 mg, 0.06 mmol, 20 mol%) and TEMPO (57 mg, 0.36 mmol, 1.2 equiv) under argon, then the mixture was stirred at room temperature for 10 minutes before TMSCF$_3$ (88 µL, 0.6 mmol, 2.0 equiv) was added. The reaction mixture was stirred at 40 °C for 4 h and monitored by TLC. Then the reaction was quenched with saturated aqueous NaHCO$_3$ solution. The mixture was first filtered through a short pad of celite (to remove the molecular sieves) and then extracted with EtOAc. The organic phase was concentrated and the crude product was purified by flash column chromatography to afford 2.
c. Procedure for Cu(II)-Catalyzed Trifluoromethylation of 1,10-Phenanthroline

**Scheme S5.** Cu(II)-Catalyzed Trifluoromethylation of 1,10-Phenanthroline to Afford 1,2-Dihydrophenanthroline

Under argon, to a mixture of 10 (18 mg, 0.1 mmol), Cu(OAc)$_2$ (3.7 mg, 0.02 mmol), KOAc (9.8 mg, 0.1 mmol) and HOAc (6 µL, 0.1 mmol) in toluene (2.0 mL), TMSCF$_3$ (15 µL, 0.1 mmol) was added at room temperature. The reaction mixture was allowed to stir at 40 °C for 3 hours. Another portion of TMSCF$_3$ (15 µL, 0.1 mmol) was added and continue stirring at 40 °C. After 24 hours, the reaction was quenched by H$_2$O and extracted with ethyl acetate for three times. The organic layer was washed by brine, dried over Na$_2$SO$_4$ and concentrated under vacuum. The residue was purified with flash silica gel column chromatography (40% ethyl acetate in petroleum ether).

2-(Trifluoromethyl)-1,2-dihydro-1,10-phenanthroline (11) :

$^1$H NMR (400 MHz, CDCl$_3$, ppm): δ 8.72 (d, $J$ = 3.2 Hz, 1H), 8.01 (d, $J$ = 8.4 Hz, 1H), 7.34 (q, $J$ = 4.0 Hz, 1H), 7.14 (d, $J$ = 8.0 Hz, 1H), 7.04 (d, $J$ = 8.4 Hz, 1H), 6.77 (d, $J$ = 10.0 Hz, 1H), 6.41 (s, 1H), 5.63 (td, $J$ = 7.6 Hz, 2.0 Hz, 1H), 5.12 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm): δ 147.9, 138.5, 136.6, 136.0, 129.0, 126.0, 125.2, 123.7 (q, $J$ = 264 Hz), 121.6, 115.1, 114.2, 113.4, 55.0 (q, $J$ = 31 Hz); $^{19}$F NMR (377 MHz, CDCl$_3$, ppm): δ -81.24 (d, $J$ = 7.5 Hz). IR $v_{\text{max}}$ (neat)/cm$^{-1}$: 3672, 2928, 2513, 2159, 2029, 1977, 1384, 1120, 1067. HRMS (ESI, m/z): calcd for C$_{13}$H$_{10}$N$_2$F$_3^+$ [M+H$^+$]: 251.0796, found: 251.0791.
E. NMR Spectra

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^{19}F$ NMR (377 MHz, CDCl$_3$)
$^{19}$F NMR (377 MHz, CDCl$_3$)
$^{19}F$ NMR (377 MHz, CDCl$_3$)

S9a
$^1$H NMR (400 MHz, CDCl$_3$)

$^13$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (377 MHz, CDCl$_3$)

R = 4-Me-phenyl

![NMR Spectrum](image)
19F NMR (377 MHz, CDCl3)