Silver-Catalyzed Cyclization of Nitrones with 2-Azetine: A Radical Approach to 2,3-Disubstituted Quinolines

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1. Substrate Preparation

Nitrones\(^1\) (listed below) and N-boc-2-azetine\(^2\) were synthesized according to the reported procedures.

1.1 General procedure for the preparation of nitrones

Nitroarene (1.0 equiv), aldehyde (1.1 equiv) and NH\(_4\)Cl (1.2 equiv) were dissolved in a 1:1 mixture of EtOH and water (2 mL/mmol of starting material) and cooled to 0 °C (ice bath). Then zinc powder (2.0 equiv) was added to the resulting mixture, and the reaction was allowed to warm to room temperature and stirred for 16 hours. The reaction mixture was filtered and washed with CH\(_2\)Cl\(_2\). The filtrate was extracted with CH\(_2\)Cl\(_2\) (4 × 50 mL) and the combined organic layer was washed with brine, dried over Na\(_2\)SO\(_4\), concentrated under reduced pressure to give crude nitrones. Pure nitrones were obtained by recrystallization from ethyl acetate (cal. 65% yield).

\[
\begin{align*}
1a: R &= H & 1e: R &= Br \\
1b: R &= OMe & 1f: R &= NO_2 \\
1c: R &= F & 1g: R &= CF_3 \\
1d: R &= Cl \\
1h: X &= O & 1n: X &= Ph \\
1i: X &= S & 1o: R &= OMe \\
1j: R &= Cl & 1q: R &= Br \\
1k: X &= OMe & 1m: X &= S \\
1l: X &= CO_2Et & 1p: R &= CO_2Et
\end{align*}
\]
1.2 General procedure for the preparation of N-Boc-2-azetine

To a solution of azetidinol SI-1 (8.00 g, 46.2 mmol) in CCl4 (50 mL) was added Ph3P (13.3 g, 50.8 mmol, 1.1 equiv) and NaHCO3 (30 mg). The reaction mixture was heated to reflux. After 17 h, the reaction mixture was cooled to rt, concentrated to dryness under reduced pressure, suspended in pet ether (50 mL) and filtered. The solid was resuspended in pet ether (50 mL) and filtered. The combined pet ether washings were concentrated to dryness under reduced pressure. Purification (Si-gel, pet ether/ethyl acetate 1:0→4:1) gave chloride SI-2 as a colorless oil (6.6 g, 75%).

To a solution of t-BuOK (440 mg, 3.92 mmol) in DMSO (5 mL) was added dropwise N-Boc-3-chloroazetidine SI-2 (500 mg, 2.61 mmol) in THF (5 mL). The reaction mixture was then heated to 70°C for 17 h, then cooled to rt. Water (10 mL) was added and the reaction mixture extracted with n-Pentane (2 × 10 mL). The combined organic layers were concentrated to dryness under reduced pressure. Purification (Si-gel, pet ether/ethyl acetate 1:0→10:1) gave azetine 2 as a colorless liquid (364 mg, 60%).
2. Screening Reaction Conditions

Table S1 summarizes in-depth condition tuning for the reaction of nitrone 1a with N-Boc-2-azetine 2.

![Diagram of the reaction](Image)

Table S1. Screening reaction conditions.[a]

<table>
<thead>
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<th>Entry</th>
<th>Additive 1/x mol%</th>
<th>Additive 2/x mol%</th>
<th>Solvent</th>
<th>t [°C]</th>
<th>Yield of 3a[b]</th>
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[a] Reaction conditions: 1a (0.25 mmol), 2 (0.5 mmol), 2.0 mL of solvent reacted for 18 h unless otherwise stated. [b] Yield of 3a was determined by HPLC analysis using naphthalene as an internal standard. [c] Isolated yield. [d] 1a (0.5 mmol), 2 (0.25 mmol).
3. Characterization of Products

3a. 81% yield, white solid, mp 112–114 °C, R_f = 0.5 (petroleum ether/ethyl acetate = 4/1); _1H NMR (400 MHz, CDCl_3) δ 8.19 (s, 1H), 8.14 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.57–7.52 (m, 3H), 7.51–7.43 (m, 3H), 4.87 (s, 1H), 4.44 (d, J = 6.2 Hz, 2H), 1.44 (s, 9H); _13C NMR (100 MHz, CDCl_3) δ 155.9, 147.1, 140.1, 135.3, 130.5, 129.6, 129.4, 128.72, 128.7, 128.6, 127.5, 127.4, 126.8, 79.9, 42.5, 28.5; HRMS (ESI, m/z) calcd for C_{21}H_{23}N_2O_2 [M + H]^+ 335.1754, found 335.1762.

3b. 80% yield, white solid, mp 104–106 °C, R_f = 0.4 (petroleum ether/ethyl acetate = 4/1); _1H NMR (400 MHz, acetone-d_6) δ 8.28 (s, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.62 (d, J = 8.4 Hz, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.07 (d, J = 8.4 Hz, 2H), 6.57 (s, 1H), 4.48 (d, J = 5.9 Hz, 2H), 3.88 (s, 3H), 1.43 (s, 9H); _13C NMR (100 MHz, acetone-d_6) δ 160.8, 159.6, 156.8, 147.9, 135.3, 133.6, 132.3, 131.3, 129.92, 129.90, 128.2, 127.1, 114.3, 79.1, 55.6, 42.9, 28.6; HRMS (ESI, m/z) calcd for C_{22}H_{25}N_2O_3 [M + H]^+ 365.1860, found 365.1862.

3c. 74% yield, white solid, mp 115–118 °C, R_f = 0.4 (petroleum ether/ethyl acetate = 4/1); _1H NMR (400 MHz, CDCl_3) δ 8.20 (s, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.71 (t, J = 7.6 Hz, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.49–7.41 (m, 1H), 7.33–7.26 (m, 2H), 7.14 (m, 1H), 4.90 (s, 1H), 4.43 (d, J = 6.1 Hz, 2H), 1.44 (s, 9H); _13C NMR (100 MHz, CDCl_3) δ 162.9 (d, J = 247.3 Hz), 158.1, 155.9, 147.1, 142.2, 135.6, 130.3 (d, J = 8.3 Hz), 129.9, 129.4, 127.6, 127.5, 127.1, 124.6 (d, J = 3.1 Hz), 116.1 (d, J = 22.6 Hz), 80.1, 42.4, 28.5; _19F NMR (377 MHz, CDCl_3) δ -112.4; HRMS (ESI, m/z) calcd for C_{21}H_{22}FN_2O_2 [M + H]^+ 353.1660, found 353.1662.
3d. 73% yield, white solid, mp 120–123 °C, Rf = 0.3 (petroleum ether/ethyl acetate = 4/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.12 (s, 1H), 8.04 (d, $J$ = 8.4 Hz, 1H), 7.77 (d, $J$ = 8.1 Hz, 1H), 7.64 (t, $J$ = 7.5 Hz, 1H), 7.48 (t, $J$ = 7.5 Hz, 1H), 7.41 (q, $J$ = 8.5 Hz, 4H), 4.78 (s, 1H), 4.36 (d, $J$ = 6.1 Hz, 2H), 1.37 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 158.3, 155.9, 147.1, 135.6, 134.9, 130.3, 129.9, 129.4, 128.9, 127.5, 127.49, 127.1, 80.1, 42.5, 28.5; HRMS (ESI, m/z) calcd for C$_{21}$H$_{22}$ClN$_2$O$_2$ [M + H]$^+$ 369.1364, found 369.1383.

3e. 78% yield, yellow solid, mp 120–123 °C, Rf = 0.35 (petroleum ether/ethyl acetate = 4/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.15 (s, 1H), 8.10 (d, $J$ = 7.6 Hz, 1H), 7.79 (t, $J$ = 5.8 Hz, 1H), 7.68 (d, $J$ = 7.7 Hz, 1H), 7.61–7.50 (m, 3H), 7.43–7.34 (m, 2H), 5.08 (s, 1H), 4.38 (d, $J$ = 6.4 Hz, 2H), 1.43 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 158.1, 155.8, 146.9, 138.8, 135.5, 131.7, 130.5, 130.2, 129.8, 129.2, 127.5, 127.4, 126.9, 123.0, 79.9, 42.3, 28.4, 28.3; HRMS (ESI, m/z) calcd for C$_{21}$H$_{22}$BrN$_2$O$_2$ [M + H]$^+$ 413.0859, found 413.0882.

3f. 70% yield, white solid, mp 131–133 °C Rf = 0.2 (petroleum ether/ethyl acetate = 4/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.35 (d, $J$ = 8.5 Hz, 2H), 8.25 (s, 1H), 8.12 (d, $J$ = 8.4 Hz, 1H), 7.91–7.86 (m, 1H), 7.80–7.73 (m, 3H), 7.60 (t, $J$ = 7.5 Hz, 1H), 4.86 (s, 1H), 4.44 (d, $J$ = 6.1 Hz, 2H), 1.43 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 157.1, 155.7, 147.9, 136.0, 130.3, 130.1, 129.5, 127.7, 127.6, 123.9, 80.3, 42.4, 28.5; HRMS (ESI, m/z) calcd for C$_{21}$H$_{22}$N$_3$O$_4$ [M + H]$^+$ 380.1605, found 380.1609.

3g. 71% yield, white solid, mp 125–128 °C Rf = 0.4 (petroleum ether/ethyl acetate = 4/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.23 (s, 1H), 8.12 (d, $J$ = 8.5 Hz, 1H), 7.87 (d, $J$ = 8.2 Hz, 1H), 7.78–7.72 (m, 3H), 7.69 (d, $J$ = 8.0 Hz, 2H), 7.58 (t, $J$ = 7.5 Hz, 1H), 4.83 (s, 1H), 4.44 (d, $J$ = 6.0 Hz, 2H), 1.44 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.5, 158.0, 155.9, 147.2, 137.5, 135.5, 133.3, 129.8, 129.5, 128.6 (q, $J$ = 270 Hz),
128.0 (q, $J = 32$ Hz), 126.9, 126.7, 126.6, 126.5, 125.0 (q, $J = 3.8$ Hz), 79.9, 42.6, 28.5; $^{19}$F NMR (377 MHz, CDCl$_3$) δ -62.6; HRMS (ESI, m/z) calcd for C$_{22}$H$_{22}$F$_3$N$_2$O$_2$ [M + H]$^+$ 403.1628, found 403.1648.

3h, 81% yield, white solid, mp 115–118 °C, R$_f$ = 0.4 (petroleum ether/ethyl acetate = 4/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.19 (s, 1H), 8.13 (d, $J = 8.5$ Hz, 1H), 7.84 (d, $J = 7.9$ Hz, 1H), 7.70 (t, $J = 7.7$ Hz, 1H), 7.54 (t, $J = 7.5$ Hz, 1H), 7.39 (t, $J = 9.1$ Hz, 1H), 7.13–7.03 (m, 2H), 6.99 (dd, $J = 8.3$, 2.5 Hz, 1H), 4.86 (s, 1H), 4.44 (d, $J = 6.2$ Hz, 2H), 3.85 (s, 3H), 1.44 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.9, 147.1, 141.4, 135.5, 130.5, 129.8, 129.7, 129.4, 127.5, 126.8, 121.0, 114.7, 114.1, 79.9, 55.5, 42.5, 28.5; HRMS (ESI, m/z) calcd for C$_{22}$H$_{25}$N$_2$O$_3$ [M + H]$^+$ 365.1860, found 365.1881.

3i, 75% yield, colourless oil, $^1$H NMR (400 MHz, CDCl$_3$) δ 8.20 (s, 1H), 8.13 (d, $J = 8.0$ Hz, 1H), 7.86 (d, $J = 7.5$ Hz, 1H), 7.71 (t, $J = 6.8$ Hz, 1H), 7.56 (t, $J = 6.4$ Hz, 1H), 7.37–7.24 (m, 4H), 4.89–4.77 (m, 1H), 4.20 (s, 2H), 2.10 (s, 3H), 1.42 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 155.9, 139.4, 135.7, 135.0, 130.9, 130.7, 129.5, 129.3, 128.6, 128.2, 127.6, 127.5, 126.8, 126.2, 79.8, 42.20, 28.5, 19.7; HRMS (ESI, m/z) calcd for C$_{22}$H$_{25}$N$_2$O$_3$ [M + H]$^+$ 349.1911, found 349.1915.

3j, 65% yield, colourless oil, R$_f$ = 0.4 (petroleum ether/ethyl acetate = 4/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.23 (s, 1H), 8.16 (d, $J = 8.5$ Hz, 1H), 8.01 (s, 1H), 7.96 (d, $J = 8.4$ Hz, 1H), 7.91–7.83 (m, 3H), 7.74–7.65 (m, 2H), 7.59–7.52 (m, 3H), 4.85 (s, 1H), 4.50 (d, $J = 6.1$ Hz, 2H), 1.41 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.5, 155.9, 147.2, 137.5, 135.5, 133.3, 130.7, 129.7, 129.7, 128.55, 128.51, 128.2, 127.9, 127.6, 127.5, 126.9, 126.7, 126.6, 126.5, 80.0, 42.6, 28.5; HRMS (ESI, m/z) calcd for C$_{25}$H$_{25}$N$_2$O$_2$ [M + H]$^+$ 385.1911, found 385.1921.
3k, 68% yield, colourless oil, R_f = 0.3 (petroleum ether/ethyl acetate = 4/1); 1H NMR (400 MHz, CDCl_3) δ 8.29 (s, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.94 (dd, J = 11.1, 8.2 Hz, 3H), 7.74 (t, J = 7.7 Hz, 1H), 7.60 (td, J = 8.1, 7.6, 5.8 Hz, 2H), 7.53–7.46 (m, 2H), 7.39–7.32 (m, 2H), 4.62 (s, 1H), 4.17 (d, J = 6.4 Hz, 2H), 1.38 (s, 9H); 13C NMR (100 MHz, CDCl_3) δ 159.0, 155.8, 147.2, 137.4, 135.2, 133.9, 131.9, 131.7, 129.7, 129.5, 129.0, 128.6, 127.7, 127.0, 126.8, 126.4, 126.3, 125.6, 125.3, 79.8, 42.2, 28.4; HRMS (ESI, m/z) calcd for C_{25}H_{23}N_2O_2 [M + H]^+ 385.1911, found 385.1928.

3l, 71% yield, white solid, mp 98–100 °C, R_f = 0.5 (petroleum ether/ethyl acetate = 4/1); 1H NMR (400 MHz, CDCl_3) δ 8.18 (s, 1H), 7.64 (d, J = 7.7 Hz, 1H), 7.42 (t, J = 6.9 Hz, 3H), 7.38–7.20 (m, 6H), 7.14 (s, 1H), 6.93 (d, J = 8.6 Hz, 2H), 3.84 (s, 3H); 13C NMR (100 MHz, CDCl_3) δ 156.0, 154.3, 147.9, 147.2, 143.9, 137.3, 129.9, 129.2, 129.0, 127.6, 127.2, 126.8, 112.5, 112.3, 79.9, 43.1, 28.6; HRMS (ESI, m/z) calcd for C_{19}H_{21}N_2O_3 [M + H]^+ 325.1547, found 325.1560.

3m, 70% yield, white solid, mp 98–100 °C, R_f = 0.5 (petroleum ether/ethyl acetate = 4/1); 1H NMR (400 MHz, CDCl_3) δ 8.18 (s, 1H), 8.08 (d, J = 8.5 Hz, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.66 (d, J = 12.6 Hz, 2H), 7.49 (s, 1H), 7.26 (s, 1H), 6.63–6.61 (m, 1H), 5.27 (s, 1H), 4.73 (d, J = 6.4 Hz, 2H), 1.45 (s, 9H); 13C NMR (100 MHz, CDCl_3) δ 156.0, 147.9, 147.2, 143.9, 137.3, 129.9, 129.8, 127.6, 126.8, 112.5, 112.3, 79.9, 43.1, 28.6; HRMS (ESI, m/z) calcd for C_{15}H_{21}N_2O_2S [M + H]^+ 341.1318, found 341.1496.

3n, 82% yield, colourless oil, R_f = 0.4 (petroleum ether/ethyl acetate =4/1); 1H NMR (400 MHz, CDCl_3) δ 8.16 (s, 1H), 7.56 (d, J = 6.6 Hz, 2H), 7.51–7.31 (m, 5H), 7.04 (d, J = 7.5 Hz, 1H), 4.80 (s, 1H), 4.45 (d, J = 6.2 Hz, 2H), 4.05 (s, 3H), 1.44 (s, 9H); 13C NMR (100 MHz, CDCl_3) δ 158.4, 156.0, 155.6, 140.3, 139.1, 135.3, 129.2, 128.6,
126.9, 119.4, 107.9, 79.9, 56.2, 42.6, 28.5; HRMS (ESI, m/z) calcd for C\textsubscript{22}H\textsubscript{25}N\textsubscript{2}O\textsubscript{3} [M + H]\(^+\) 365.1860, found 365.1874.

![Structure 3o](attachment:image.png)

3o, 83% yield, colourless oil, R\(_f\) = 0.4 (petroleum ether/ethyl acetate = 4/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.09 (s, 1H), 8.02 (d, \(J = 9.2\) Hz, 1H), 7.54–7.42 (m, 5H), 7.35 (dd, \(J = 9.2, 2.7\) Hz, 1H), 7.09 (t, \(J = 2.4\) Hz, 1H), 4.87 (s, 1H), 4.42 (d, \(J = 6.2\) Hz, 2H), 3.93 (s, 3H), 1.44 (s, 9H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.9, 156.9, 143.1, 140.0, 134.2, 130.7, 128.7, 128.6, 128.3, 122.3, 104.8, 79.8, 55.6, 42.4, 28.4; HRMS (ESI, m/z) calcd for C\textsubscript{22}H\textsubscript{25}N\textsubscript{2}O\textsubscript{3} [M + H]\(^+\) 365.1860, found 365.1872.

![Structure 3p](attachment:image.png)

3p, 72% yield, white solid, mp 100–102, R\(_f\) = 0.3 (petroleum ether/ethyl acetate = 4/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.11 (s, 1H), 8.06 (d, \(J = 9.0\) Hz, 1H), 7.83 (d, \(J = 2.3\) Hz, 1H), 7.63 (dd, \(J = 9.0, 2.4\) Hz, 1H), 7.54–7.45 (m, 5H), 4.85 (s, 1H), 4.44 (d, \(J = 6.3\) Hz, 2H), 1.45 (s, 9H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 159.8, 155.9, 145.5, 139.7, 134.3, 132.5, 131.7, 131.1, 130.6, 128.9, 128.7, 128.1, 126.2, 80.1, 42.5, 28.5; HRMS (ESI, m/z) calcd for C\textsubscript{21}H\textsubscript{22}ClN\textsubscript{2}O\textsubscript{2} [M + H]\(^+\) 369.1364, found 369.1373.

![Structure 3q](attachment:image.png)

3q, 71% yield, white solid, mp 111–114, R\(_f\) = 0.4 (petroleum ether/ethyl acetate = 4/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.63 (s, 1H), 8.30 (d, \(J = 7.7\) Hz, 2H), 8.17 (d, \(J = 8.8\) Hz, 1H), 7.59–7.48 (m, 5H), 4.85 (s, 1H), 4.44 (d, \(J = 6.2\) Hz, 2H), 1.45 (s, 9H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 166.3, 161.6, 155.9, 145.7, 139.7, 134.2, 131.3, 131.7, 129.5, 128.9, 128.8, 128.7, 128.6, 120.7, 80.1, 42.5, 28.5; HRMS (ESI, m/z) calcd for C\textsubscript{21}H\textsubscript{22}BrN\textsubscript{2}O\textsubscript{2} [M + H]\(^+\) 413.0859, found 413.0858.

![Structure 3r](attachment:image.png)

3r, 55% yield, white solid, mp 106–108, R\(_f\) = 0.3 (petroleum ether/ethyl acetate = 4/1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.63 (s, 1H), 8.30 (d, \(J = 7.7\) Hz, 2H), 8.17 (d, \(J = 8.8\) Hz, 1H), 7.59–7.48 (m, 5H), 4.85 (s, 1H), 4.44 (d, \(J = 6.2\) Hz, 2H), 1.46 (s, 9H), 1.34–1.23 (m, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 166.3, 161.6, 155.9, 148.9, 139.7,
136.3, 130.6, 132.9, 129.2, 128.9, 128.8, 128.7, 128.0, 126.6, 80.4, 61.5, 42.4, 28.5, 14.5; HRMS (ESI, m/z) calcd for C<sub>24</sub>H<sub>27</sub>N<sub>2</sub>O<sub>4</sub> [M + H]<sup>+</sup> 407.1965, found 407.1971.

3s and 3s', 66% yield, 3s:3s' = 2:1, white solid, mp 100–102 °C, R<sub>f</sub> = 0.3 (petroleum ether/ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.35 (s, 0.69 H), 8.15 (s, 0.33 H), 7.99 (d, <i>J</i> = 8.5 Hz, 0.71 H), 7.92 (s, 0.32 H), 7.73 (d, <i>J</i> = 8.3 Hz, 0.34 H), 7.60–7.45 (m, 5.66 H), 7.38 (t, <i>J</i> = 5.6 Hz, 1.03 H), 4.84 (s, 0.96 H), 4.45 (dd, <i>J</i> = 15.3, 6.2 Hz, 2H), 2.72 (s, 2H), 2.56 (s, 1H), 1.45 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 159.5, 159.0, 156.0, 147.4, 140.3, 140.2, 140.0, 135.2, 134.3, 132.0, 129.9, 129.4, 129.1, 128.79, 128.75, 128.71, 128.68, 128.61, 128.56, 128.4, 127.7, 127.2, 126.8, 79.89, 42.7, 28.5, 22.1, 18.8; HRMS (ESI, m/z) calcd for C<sub>22</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub> [M + H]<sup>+</sup> 349.1911, found 349.1985.

3t, 80% yield, colorless oil, R<sub>f</sub> = 0.4 (petroleum ether/ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.04 (s, 1H), 7.99 (d, <i>J</i> = 9.2 Hz, 1H), 7.48–7.42 (m, 2H), 7.32 (dd, <i>J</i> = 9.2, 2.8 Hz, 1H), 7.05 (d, <i>J</i> = 2.8 Hz, 1H), 7.01–6.93 (m, 2H), 4.94 (s, 1H), 4.42 (d, <i>J</i> = 6.1 Hz, 2H), 3.91 (s, 3H), 3.83 (s, 3H), 1.43 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 159.8, 157.9, 156.7, 143.2, 134.2, 132.6, 130.7, 130.2, 128.2, 122.3, 114.1, 104.9, 79.8, 55.6, 55.5, 42.6, 28.5; HRMS (ESI, m/z) calcd for C<sub>23</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub> [M + H]<sup>+</sup> 395.1965, found 395.1986.

3u, 70% yield, colorless oil, R<sub>f</sub> = 0.25 (petroleum ether/ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.11 (s, 1H), 8.00 (d, <i>J</i> = 9.2 Hz, 1H), 7.74 (d, <i>J</i> = 8.1 Hz, 2H), 7.66 (d, <i>J</i> = 8.0 Hz, 2H), 7.37 (dd, <i>J</i> = 9.2, 2.8 Hz, 1H), 7.10 (d, <i>J</i> = 2.8 Hz, 1H), 4.86 (s, 1H), 4.42 (d, <i>J</i> = 6.1 Hz, 2H), 3.95 (s, 3H), 1.44 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 158.4, 155.9, 155.4, 143.8, 143.3, 134.6, 130.9 (q, <i>J</i> = 270 Hz), 130.4, 129.4, 128.7, 125.7, 125.62 (q, <i>J</i> = 3.8 Hz), 122.9, 104.9, 80.1, 55.7, 42.4, 28.5; HRMS (ESI, m/z) calcd for C<sub>23</sub>H<sub>24</sub>F<sub>3</sub>N<sub>2</sub>O<sub>3</sub> [M + H]<sup>+</sup> 433.1734, found 433.1756.
3v, 62% yield, white solid, mp 160–163 °C, R<sub>f</sub> = 0.2 (petroleum ether/ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.59 (d, <i>J</i> = 1.8 Hz, 1H), 8.28 (d, <i>J</i> = 8.0 Hz, 2H), 8.14 (d, <i>J</i> = 8.8 Hz, 1H), 7.53 (d, <i>J</i> = 8.2 Hz, 2H), 7.02 (d, <i>J</i> = 8.3 Hz, 2H), 4.92 (s, 1H), 4.47 (dq, <i>J</i> = 14.3, 7.1, 6.5 Hz, 4H), 3.87 (s, 3H), 1.46 (t, <i>J</i> = 4.7 Hz, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 166.2, 160.2, 148.8, 136.2, 131.9, 131.5, 130.4, 130.1, 129.4, 128.9, 128.24, 126.3, 114.1, 79.9, 61.3, 55.4, 42.4, 28.4, 14.4; HRMS (ESI, m/z) calcd for C<sub>25</sub>H<sub>29</sub>N<sub>2</sub>O<sub>5</sub> [M + H]<sup>+</sup> 437.2071, found 437.2074.

4b, 92% yield, white solid, mp 80–83 °C, R<sub>f</sub> = 0.6 (petroleum ether/ethyl acetate = 4/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.16–7.12 (m, 2H), 7.08 (dd, <i>J</i> = 8.7, 7.1 Hz, 2H), 6.99 (d, <i>J</i> = 8.2 Hz, 2H), 6.78–6.70 (m, 3H), 5.93 (d, <i>J</i> = 25.9 Hz, 1H), 4.95 (s, 1H), 3.74 (dd, <i>J</i> = 8.2, 7.3 Hz, 1H), 3.65 (s, 3H), 3.47–3.42 (m, 1H), 3.34 (s, 1H), 1.44 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 158.9, 153.7, 150.3, 132.2, 128.5, 127.9, 121.1, 114.0, 92.9, 80.4, 69.3, 55.3, 49.3, 28.5; HRMS (ESI, m/z) calcd for C<sub>22</sub>H<sub>27</sub>N<sub>2</sub>O<sub>4</sub> [M + H]<sup>+</sup> 383.1965, found 383.1977.
4. Control Experiments

Scheme S1. Summary of control experiments
Scheme S1-1. The effect of radical inhibitor

This reaction was performed following the “General Procedure”, only except that 20 mol% or 2.0 equiv TEMPO was added. The desired product \(3b\) was not observed, suggesting that a radical-mediated pathway might be involved.

Scheme S1-2. Isolation of intermediate \(4b\) and its further transformation to \(3b\)

Nitrone \(1b\) (0.25 mmol) and 2.0 mL of solvent toluene was weighted and placed in a dried Schlenk tube, followed by the \(N\)-Boc-2-azetine \(2\) (0.5 mmol, 2 equiv). The reaction mixture was stirred at 40 °C for 10 h. After cooling to room temperature, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the intermediate \(4b\). The product was isolated in 92% yield.

\(\text{AgOTf} (0.025 \text{ mmol}, 6.4 \text{ mg}, 10 \text{ mol%}), \text{ intermediate} \ 4b \ (0.25 \text{ mmol}) \) and 2.0 mL of solvent toluene were weighted in the glove box and placed in a dried Schlenk tube. The reaction mixture was stirred at 40 °C for 18 h. After cooling to room temperature, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the desired product \(3b\) in 85% yield.
Scheme S1-3. Reaction of 1b-\textit{d}5 with 2

\[
\begin{align*}
\text{H} & \quad \text{OMe} \\
\text{D} & \quad \text{D} \\
\text{D} & \quad \text{D} \\
\text{D} & \quad \text{D} \\
\hline
\text{N} & \quad \text{O} \\
\text{N} & \quad \text{Boc} \\
\text{N} & \quad \text{Boc} \\
\text{N} & \quad \text{Boc} \\
\text{N} & \quad \text{Boc}
\end{align*}
\]

This reaction was performed following the “General Procedure”, only except that 1b-\textit{d}5 was used as nitrone.

Scheme S1-4. Reaction of 1b with 2-\textit{d}1

\[
\begin{align*}
\text{H} & \quad \text{OMe} \\
\text{Ph} & \quad \text{N} & \quad \text{O} \\
\text{D} & \quad \text{N} & \quad \text{Boc} \\
\text{D} & \quad \text{N} & \quad \text{Boc} \\
\text{D} & \quad \text{N} & \quad \text{Boc}
\end{align*}
\]

This reaction was performed following the “General Procedure”, only except that 2-\textit{d}1 was used. Compared with the \textit{1}H NMR spectra of 3b, the deuterium atom was completely transferred into the product (>95% deuterium incorporation).

Scheme S1-5. Intermolecular competitive reactions

\[
\begin{align*}
\text{H} & \quad \text{OMe} \\
\text{D} & \quad \text{D} \\
\text{D} & \quad \text{D} \\
\text{D} & \quad \text{D} \\
\hline
\text{N} & \quad \text{O} \\
\text{N} & \quad \text{Boc} \\
\text{N} & \quad \text{Boc} \\
\text{N} & \quad \text{Boc} \\
\text{N} & \quad \text{Boc}
\end{align*}
\]

AgOTf (0.025 mmol, 6.4 mg, 10 mol%), nitrone 1b (0.25 mmol), nitrone 1b-\textit{d}5 were weighted in the glove box and placed in a dried Schlenk tube. Then 2.0 mL of solvent toluene was added, followed by the N-Boc-2-azetine 2 (0.5 mmol, 2 equiv). The reaction mixture was stirred at 40 °C for 5 h. After cooling to room temperature, the solvent was evaporated and the crude product was directly purified by silica gel column chromatography to give the mixture of 3b and 3b-\textit{d}4. A PIE value of 1.0 was obtained on the basis of \textit{1}H NMR analysis.
Scheme S1-5. Competition reaction between 1o and 1r

AgOTf (0.025 mmol, 6.4 mg, 10 mol%), nitrono 1o (0.25 mmol), nitrone 1r were weighted in the glove box and placed in a dried Schlenk tube. Then 2.0 mL of solvent toluene was added, followed by the N-Boc-2-azetine 2 (0.5 mmol, 2 equiv). The reaction mixture was stirred at 40 °C for 18 h. After cooling to room temperature, the solvent was evaporated and the crude product was directly purified by silica gel column chromatography to give the product 3o and 3r respectively. The isolated yield ratio of 3o:3r was 12:1.
5. EPR spectra of Ag-catalyzed transformations
6. Crystal Structure of Products

ORTEP drawing of 3e (CCDC1526502) with thermal ellipsoids at the 50% probability

Table S1. Crystal data and structure refinement for cd16158m_a.

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<td>Crystal system</td>
<td>Triclinic</td>
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<td>Space group</td>
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<tr>
<td></td>
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<td>Absorption correction</td>
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<td>Max. and min. transmission</td>
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<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
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Data / restraints / parameters 3288 / 78 / 249
Goodness-of-fit on F² 0.963
Final R indices [I>2sigma(I)]
R1 = 0.0911, wR2 = 0.2098
R indices (all data)
R1 = 0.2545, wR2 = 0.2887
Largest diff. peak and hole 0.494 and -0.436 e.Å⁻³

ORTEP drawing of 3e (CCDC1526503) with thermal ellipsoids at the 50% probability

**Table S2.** Crystal data and structure refinement for cd16586.

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<td></td>
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<td>Absorption correction</td>
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<td>Max. and min. transmission</td>
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<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
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S18
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<td>Largest diff. peak and hole</td>
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7. References
8. Copies of NMR Spectra

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

3a

Copies of NMR Spectra
$^{13}$C NMR (100MHz, CDCl$_3$)
$^1$H NMR (400MHz, Acetone-$d_6$)
$^{13}$C NMR (100MHz, Acetone-$d_6$)
$^{19}$F NMR (377MHz, CDCl$_3$)

$3c$

S27
$^{13}$C NMR (100MHz, CDCl$_3$)
$^1$H NMR (400MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^{1}$H NMR (400MHz, CDCl$_3$)
$^{19}$F NMR (377 MHz, CDCl$_3$)

$3g$
$^{1}$H NMR (400MHz, CDCl$_3$)
$^{13}$C NMR (100 MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^1$H NMR (400MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^1$H NMR (400MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^1$H NMR (400MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^1$H NMR (400MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^{1}$H NMR (400MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^{1}$H NMR (400MHz, CDCl$_3$)

3r

EtOOC

NH

H

Ph

S57
$^{13}$C NMR ($100$MHz, CDCl$_3$)
$3s:3s' = 2:1$

$^1H$ NMR (400MHz, CDCl$_3$)
$3s \cdot 3s' = 2:1$

$^{13}$C NMR (100MHz, CDCl$_3$)
$^{1}$H NMR (400MHz, CDCl$_3$)
\[ 13C \text{ NMR (100MHz, CDCl}_3) \]

3t

MeO

NH\text{Boc}

OMe
3u

$^1$H NMR (400MHz, CDCl$_3$)
$^{13}$C NMR (100MHz, CDCl$_3$)
$^{19}$F NMR (377MHz, CDCl$_3$)
\[ \text{EtOOC} \quad \text{NH\textsubscript{Boc}} \quad \text{OMe} \]

\[ 3v \]

$^{13}\text{C NMR (100MHz, CDCl}_3)$
^1H NMR (400 MHz, CDCl\textsubscript{3})

4b
$^{13}$C NMR (100MHz, CDCl$_3$)