Metal-Free C-H Alkylation of Heteroarenes with Alkyltrifluoroborates: A General Protocol for 1°, 2°, and 3° Alkylation

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GENERAL CONSIDERATIONS:

NMR Spectra (\(^1\)H, \(^{13}\)C, \(^{19}\)F) were performed at 298 K. \(^1\)H NMR spectra were referenced to residual non-deuterated chloroform (\(\delta\) 7.26) in CDCl\(_3\), residual DMSO-\(d_6\) (\(\delta\) 2.50) in DMSO-\(d_6\), acetone-\(d_6\) (\(\delta\) 2.09) in acetone-\(d_6\), and residual MeCN-\(d_2\) (\(\delta\) 1.94) in MeCN-\(d_3\). \(^{13}\)C NMR spectra were referenced to CDCl\(_3\) (\(\delta\) 77.2) and DMSO-\(d_6\) (\(\delta\) 39.5). Reactions were monitored by HPLC, GC/MS, \(^1\)H NMR, and/or by TLC on silica gel plates (60 Å porosity, 250 µm thickness). TLC analysis was performed using hexanes/EtOAc as the eluant and visualized using UV light. Silica plugs utilized flash silica gel (60 Å porosity, 32–63 µm). Flash chromatography was accomplished using an automated system (visualizing at 254 nm, monitoring at 280 nm) with silica cartridges (60 Å porosity, 20–40 µm). Solvents were purified by use of drying cartridges through a solvent delivery system. Melting points (°C) are uncorrected.

Deuterated NMR solvents were either used as purchased (DMSO-\(d_6\)) or were stored over 4Å molecular sieves and/or K\(_2\)CO\(_3\) (CDCl\(_3\)). Na\(_2\)SO\(_4\), MgSO\(_4\), MeOH, CH\(_2\)Cl\(_2\), MeCN, pentane, Et\(_2\)O, trifluoroacetic acid, and K\(_2\)S\(_2\)O\(_8\) were used as purchased. Heteroarenes were purchased from commercial suppliers and used without further purification. MeCN/H\(_2\)O was degassed thoroughly with N\(_2\) and stored under N\(_2\). The photocatalyst \(N\)-Me-9-mesityl acridinium tetrafluoroborate was donated by Pfizer and used without further purification.
GENERAL PROCEDURE

To a 4.0 mL vial, alkyltrifluoroborate (0.30 mmol, 1.0 equiv), heteroarene (0.30 mmol, 1.0 equiv), photocatalyst (6.2 mg, 0.015 mmol, 0.05 equiv), and K$_2$S$_2$O$_8$ (162.2 mg, 0.60 mmol, 2.0 equiv) were added. Open to air, a mixture of 3.0 mL MeCN/H$_2$O (1:1) was added, followed by trifluoroacetic acid (34.2 mg, 0.30 mmol, 1.0 equiv). The mixture was stirred under 26 W CFLs (GE FLE26HT3/2/D) for 5–48 h under a fan. The reaction mixture was quenched with saturated NaHCO$_3$ and extracted with CH$_2$Cl$_2$ (3 x 20 mL). The organic extracts were combined and concentrated on Celite. The crude mixture was purified by silica gel column chromatography.

HETEROARENE SCOPE WITH TERT-BUTYLTRIFLUOROBORATE

2-(tert-Butyl)quinoline (1a)

Physical state: 40 mg, 72% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.07 (d, $J = 8.6$ Hz, 2H), 7.77 – 7.75 (m, 1H), 7.68 – 7.64 (m, 1H), 7.54 – 7.52 (m, 1H), 7.49 – 7.46 (m, 1H), 1.48 (s, 9H).
\[ ^{13}C \text{ NMR} \ (126 \text{ MHz, } \text{CDCl}_3) \delta 169.4, 147.6, 136.0, 129.6, 129.1, 127.4, 126.6, 125.7, 118.3, 38.3, 30.3. \]

HRMS (ES+) \( m/z \) calc. for \( \text{C}_{13}\text{H}_{16}\text{N} \ [\text{M+H}] 186.1283 \), found 186.1280.

FT-IR (cm\(^{-1}\), neat, ATR) 2961, 1619, 1601, 1565, 1504, 1364, 1138, 1103, 829, 756, 478.

\begin{center}
\includegraphics[width=0.2\textwidth]{2-(tert-Butyl)-4-methylquinoline.png}
\end{center}

2-(tert-Butyl)-4-methylquinoline (1b)


**Physical state:** 57 mg, 95% yield, clear oil.

\[ ^1\text{H NMR} \ (500 \text{ MHz, } \text{CDCl}_3) \delta 8.05 \ (d, J = 8.4 \text{ Hz}, 1H), 7.93-7.90 \ (m, 1H), 7.66-7.64 \ (m, 1H), 7.49-7.27 \ (m, 1H), 7.34 \ (s, 1H), 2.67 \ (s, 3H), 1.47 \ (s, 9H). \]

\[ ^{13}C \text{ NMR} \ (126 \text{ MHz, } \text{CDCl}_3) \delta 169.1, 147.5, 143.7, 130.1, 128.8, 126.7, 125.5, 123.5, 119.0, 38.1, 30.3, 19.1. \]

\begin{center}
\includegraphics[width=0.2\textwidth]{4-Bromo-2-(tert-butyl)quinoline.png}
\end{center}

4-Bromo-2-(tert-butyl)quinoline (1c)

**Physical state:** 68 mg, 86% yield, clear oil.

\[ ^1\text{H NMR} \ (500 \text{ MHz, } \text{CDCl}_3) \delta 8.10 \ (d, J = 8.4 \text{ Hz}, 1H), 8.06-8.02 \ (m, 1H), 7.79 \ (s, 1H), 7.69 \ (dd J = 7.7, 7.6 \text{ Hz}, 1H), 7.54 \ (dd, J = 7.7, 7.6 \text{ Hz}, 1H), 1.45 \ (s, 9H). \]

\[ ^{13}C \text{ NMR} \ (126 \text{ MHz, } \text{CDCl}_3) \delta 169.5, 148.3, 134.0, 130.1, 130.0, 127.0, 126.5, 126.2, 122.5, 38.3, 30.2. \]

HRMS (ES+) \( m/z \) calc. for \( \text{C}_{13}\text{H}_{12}\text{BrN} \ [\text{M+H}] 264.0388 \), found 264.0397.

FT-IR (cm\(^{-1}\), neat, ATR) 2957, 1585, 1488, 820, 756.
2-(tert-Butyl)-4-chloro-8-(trifluoromethyl)quinoline (1d)

Physical state: 78 mg, 70% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.38 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 7.2$ Hz, 1H), 7.68 (s, 1H), 7.61-7.59 (m, 1H), 1.47 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 170.5, 144.9, 142.6, 128.5 (q, $J = 5.5$ Hz), 128.3 (q, $J = 29.1$ Hz), 128.2, 125.3, 125.2, 123.1, 119.3, 38.9, 29.9.

HRMS (ES+) m/z calc. for C$_{14}$H$_{14}$ClF$_3$N [M+H] 288.0767, found 288.0762.

FT-IR (cm$^{-1}$, neat, ATR) 2965, 1592, 1489, 1463, 1293, 1145, 1118, 766.

3-(tert-Butyl)-1H-indazole (1e)


Physical state: 41 mg, 80% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 10.07 (bs, 1H), 7.91 (d, $J = 8.2$ Hz, 1H), 7.44 (d, $J = 8.2$ Hz, 1H), 7.36-7.33 (m, 1H), 7.14-7.11 (m, 1H), 1.55 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 154.8, 142.1, 126.3, 122.3, 120.7, 120.0, 110.1, 34.0, 30.2.

HRMS (ES+) m/z calc. for C$_{11}$H$_{15}$N$_2$ [M+H] 175.1235, found 175.1229.

FT-IR (cm$^{-1}$, neat, ATR) 3146, 3112, 3073, 2963, 2928, 2900, 1342, 739.
Methyl 1-(tert-Butyl)isoquinoline-3-carboxylate (1g)

**Physical state:** 55 mg isolated, 77% yield, white solid (mp = 55 °C).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 11.64 (s, 1H), 8.50 – 8.45 (m, 2H), 7.72 – 7.70 (m, 2H), 4.06 (s, 3H), 1.64 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 171.8, 158.0, 155.4, 129.6, 129.3, 129.0, 128.8, 127.3, 124.3, 118.4, 52.9, 39.7, 31.2.

HRMS: submitted.

FT-IR (cm$^{-1}$, neat, ATR) 2953, 1661, 1450, 1337, 1242, 1164.

![Structure of 1g](image)

2-(tert-Butyl)quinoxaline (1h)

**Physical state:** 39 mg, 70% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.99 (s, 1H), 8.06 (dd, $J$ = 8.0, 3.8 Hz, 2H), 7.71 (m, 2H), 1.52 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 163.8, 143.6, 141.8, 141.0, 129.8, 129.5, 129.1, 129.0, 37.4, 29.9.

HRMS (ES+) m/z calc. for C$_{12}$H$_{15}$N$_2$ [M+H] 186.1157, found 186.1158.

FT-IR (cm$^{-1}$, neat, ATR) 2963, 1558, 1492, 1464, 1365, 1237, 1155, 1128, 1097, 1014, 968, 761, 607.

![Structure of 1h](image)

2-(tert-Butyl)-3-chloroquinoxaline (1i)

**Physical state:** 28 mg isolated, 43% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.99 (s, 1H), 8.07 – 8.05 (m, 2H), 7.74 – 7.68 (m, 2H), 1.52 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 163.8, 143.6, 141.8, 141.0, 129.8, 129.5, 129.1, 129.0, 37.4, 29.9.
HRMS (ES+) m/z calc. for C_{12}H_{15}ClN_{2} [M+H] 221.0846, found 221.0844.

FT-IR (cm\(^{-1}\), neat, ATR) 2977, 1167, 1104, 1008, 761.

6-(tert-Butyl)nicotinonitrile (1j)

**Physical state:** 42 mg, 89% yield, yellow oil.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.82 (s, 1H), 7.87 (d, \(J = 8.2\) Hz, 1H), 7.46 (d, \(J = 8.2\) Hz, 1H), 1.38 (s, 9H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 174.1, 151.7, 139.5, 119.3, 117.3, 106.9, 38.4, 30.0.

HRMS (ES+) m/z calc. for C_{10}H_{13}N_{2} [M+H] 161.1079, found 161.1078.

FT-IR (cm\(^{-1}\), neat, ATR) 2960, 2050, 1721, 1596.

2-(tert-Butyl)-4-(trifluoromethyl)pyridine (1k)


**Physical state:** 58 mg, 95% yield, light yellow oil.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.74 (d, \(J = 4.9\) Hz, 1H), 7.53 (s, 1H), 7.31 (d, \(J = 5.0\) Hz, 1H), 1.40 (d, \(J = 1.9\) Hz, 9H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 171.2, 149.7, 138.7 (q, \(J = 34.0\) Hz), 123.4 (q, \(J = 271.0\)), 116.4 (q, \(J = 4.0\) Hz), 114.8, 114.81, 38.0, 30.2.

\(^{19}\)F NMR (477 MHz) \(\delta\) -64.70.

1,1'-(4-(tert-Butyl)pyridine-2,6-diyl)bis(ethan-1-one) (1l)
Physical state: 48 mg, 73% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.22 (s, 2H), 2.78 (s, 6H), 1.36 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 200.1, 162.9, 153.0, 122.0, 35.6, 30.6, 25.9.

HRMS (ES+) m/z calc. for C$_{13}$H$_{18}$NO$_2$ [M+H] 220.1338, found 220.1334.

FT-IR (cm$^{-1}$, neat, ATR) 2968, 2975, 1700, 1362, 1244, 1131, 610.

8-(tert-Butyl)-1,3,7-trimethyl-3,7-dihydro-1H-purine-2,6-dione (1m)

Physical state: 52 mg, 70% yield, white solid (173 ºC).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.11 (s, 3H), 3.56 (s, 3H), 3.39 (s, 3H), 1.47 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 160.1, 155.8, 151.9, 147.1, 108.4, 34.3, 34.2, 29.7, 29.1, 28.0.

HRMS (ES+) m/z calc. for C$_{12}$H$_{19}$N$_4$O$_2$ [M+H] 251.1508, found 251.1505.

FT-IR (cm$^{-1}$, neat, ATR) 2974, 1699, 1656, 1543, 1492, 1428, 1364, 1240, 740.

2-(tert-Butyl)nicotinamide (1n)


Physical state: 36 mg, 67% yield, light yellow solid (mp = 94 ºC).

$^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ 8.95 (d, $J$ = 2.3 Hz, 1H), 8.17 – 7.99 (m, 2H), 7.51 (d, $J$ = 8.2 Hz, 2H), 1.31 (s, 9H).

$^{13}$C NMR (126 MHz, DMSO) $\delta$ 171.2, 166.5, 147.6, 135.6, 127.0, 118.5, 20.8, 14.1.
HRMS (ES+) m/z calc. for C_{10}H_{15}N_{2}O [M+H] 179.1184, found 179.1190.

FT-IR (cm\(^{-1}\), neat, ATR) 3433, 2253, 2127, 1667, 1394, 1051, 1023, 820, 760.

2-(tert-Butyl)benzo[d]thiazole (1o)

Physical state: 38 mg, 66% yield, yellow oil.

\(^{1}\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.00 (d, \(J = 8.2\) Hz, 1H), 7.85 (d, \(J = 7.9\) Hz, 1H), 7.46 – 7.43 (m, 1H), 7.35 – 7.32 (m, 1H), 1.53 (s, 9H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 182.0, 153.4, 135.1, 125.9, 124.6, 122.8, 121.6, 38.5, 30.9.

HRMS (ES+) m/z calc. for C_{11}H_{14}NS [M+H] 192.0847, found 192.0847.

FT-IR (cm\(^{-1}\), neat, ATR) 2965, 1513, 1438, 1044, 1008, 758.

2-(tert-Butyl)quinazolin-4(3H)-one (1p)


Physical state: 54 mg, 90% yield, white solid (mp = 110–113 °C).

\(^{1}\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 11.40 (s, 1H), 8.29 (d, \(J = 7.6\) Hz, 1H), 7.74 (d, \(J = 9.8\) Hz, 2H), 7.45 (t, \(J = 7.6\) Hz, 1H), 1.50 (s, 9H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 164.1, 162.3, 149.4, 134.6, 127.8, 126.4, 126.3, 120.7, 100.1, 37.6, 28.4.

HRMS (ES+) m/z calc. for C_{12}H_{15}N_{2}O [M+H] 203.1184, found 203.1183.

FT-IR (cm\(^{-1}\), neat, ATR) 3189, 3079, 2968, 1667, 1611, 772.
N-Benzyl-2-(tert-butyl)-7H-purin-6-amine (1q)

**Physical state:** 67 mg, 79% yield, yellow solid (mp = 125–127 °C).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.45 (s, 1H), 7.44 – 7.41 (m, 2H), (dd, $J = 7.5, 7.5$ Hz, 2H), 7.29 (d, $J = 7.5$ Hz, 1H), 6.12 (bs, 1H), 4.89 (s, 2H), 1.53 (s, 9H) (highlighted proton not observed).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 160.7, 154.2, 151.6, 138.7, 128.8, 128.7, 128.2, 127.6, 100.1, 33.9, 29.6, 27.8.

HRMS (ES+) m/z calc. for C$_{16}$H$_{20}$N$_{5}$ [M+H] 282.1719, found 282.1718.

FT-IR (cm$^{-1}$, neat, ATR) 2972, 1619, 1598, 1351, 1299.

(1R)-(2-(tert-Butyl)-6-methoxyquinolin-4-yl)(5-vinluclidin-2-yl)methanol (1r)


**Physical state:** 62 mg, 54% yield, light yellow oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.98 (d, $J = 9.2$ Hz, 1H), 7.67 (s, 1H), 7.30 (d, $J = 9.2$ Hz, 1H), 7.20 (s, 1H), 5.73 (dt, $J = 17.6, 9.0$ Hz, 1H), 5.58 (s, 1H), 4.97 – 4.90 (m, 2H), 3.89 (s, 3H), 3.50 – 3.45 (m, 1H), 3.20 – 3.08 (m, 2H), 2.71 – 2.65 (m, 2H), 2.29 – 2.25 (m, 1H), 1.81 (s, 1H), 1.79 – 1.65 (m, 2H), 1.52 – 1.43 (m, 1H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 166.6, 157.4, 146.9, 143.8, 142.0, 131.9, 124.7, 120.9, 115.5, 114.6, 101.3, 72.6, 60.1, 57.3, 55.8, 43.5, 40.1, 38.1, 30.3, 28.1, 27.8, 21.6.

HRMS (ES+) m/z calc. for C$_{24}$H$_{32}$N$_{2}$O$_2$ [M+H] 381.2536, found 381.2543.
FT-IR (cm\(^{-1}\), neat, ATR) 2954, 1621, 1601, 1505, 1471, 1363, 1343, 1263, 1231, 1106, 1034, 911, 832, 734, 645.

**SECONDARY AND TERTIARY ALKYLTRIFLUOROBORATE SCOPE**

![Diagram](https://via.placeholder.com/150)

Methyl 1-(1-(Benzyloxy)-3-phenylpropyl)isoquinoline-3-carboxylate (2a)

**Physical state:** 71 mg, 58% yield, clear oil.

\(^1H\) NMR (500 MHz, CDCl\(_3\)) \(\delta 8.88 (d, J = 8.5 \text{ Hz}, 1\text{H}), 8.52 (s, 1\text{H}), 7.98 (d, J = 8.0 \text{ Hz}, 1\text{H}), 7.78 - 7.76 (m, 1\text{H}), 7.70 - 7.66 (m, 1\text{H}), 7.41 - 7.35 (m, 1\text{H}), 7.31 - 7.22 (m, 7\text{H}), 7.19 - 7.12 (m, 2\text{H}), 5.26 - 5.22 (m, 1\text{H}), 4.52 - 4.43 (m, 2\text{H}), 4.08 (s, 3\text{H}), 3.12 - 2.96 (m, 1\text{H}), 2.78 - 2.72 (m, 1\text{H}), 2.61 - 2.53 (m, 1\text{H}), 2.33 - 2.25 (m, 1\text{H}).

\(^{13}C\) NMR (126 MHz, CDCl\(_3\)) \(\delta 166.4, 161.5, 141.7, 140.2, 138.1, 136.5, 130.6, 129.1, 128.8, 128.4, 128.2, 128.1(9), 127.8, 127.7, 127.5, 126.2, 125.7, 124.8, 85.1, 71.5, 52.8, 37.8, 32.5.

HRMS (ES\(^+\)) m/z calc. for C\(_{27}\)H\(_{25}\)NO\(_3\)Na [M+Na] 434.1732, found 434.1734.

FT-IR (cm\(^{-1}\), neat, ATR) 3052, 2950, 1736, 1717, 1373, 1147, 1027, 908, 782, 490.

![Diagram](https://via.placeholder.com/150)

Methyl 1-(4,4-Difluorocyclohexyl)isoquinoline-3-carboxylate (2b)

**Physical state:** 32 mg, 35% yield, yellow oil.

\(^1H\) NMR (500 MHz, CDCl\(_3\)) \(\delta 8.43 (s, 1\text{H}), 8.22 (d, J = 7.8 \text{ Hz}, 1\text{H}), 7.98 - 7.95 (m, 1\text{H}), 7.77 - 7.72 (m, 2\text{H}), 4.02 (s, 3\text{H}), 3.72 - 3.58 (m, 1\text{H}), 2.40 - 2.27 (m, 4\text{H}), 2.16 - 1.90 (m, 4\text{H}).

\(^{13}C\) NMR (126 MHz, CDCl\(_3\)) \(\delta 166.7, 163.5, 163.5, 140.6, 136.1, 130.4, 129.4, 129.4, 129.3, 127.6, 125.2, 124.5, 123.3, 122.9, 121.4, 52.7, 39.7, 33.9, 33.7, 33.7, 33.5, 28.3, 28.2.
$^{19}$F NMR (471 MHz, C$_6$D$_6$) $\delta$ 2.26 (d, $J = 235.5$ Hz), 6.03 (d, $J = 235.5$ Hz).

HRMS (ES+) m/z calc. for C$_{17}$H$_{17}$F$_2$NO$_3$ [M+Na] 328.1125, found 328.1124.

FT-IR (cm$^{-1}$, neat, ATR) 2951, 1736, 1450, 1374, 1236, 1205, 1101, 956, 784.

Methyl 1-(Tetrahydro-2H-pyran-4-yl)isoquinoline-3-carboxylate (2c)

Physical state: 60 mg, 74% yield, white semi-solid.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.45 (s, 1H), 8.35–8.22 (m, 1H), 8.07–7.90 (m, 1H), 7.76 (dt, $J = 5.4$, 3.2 Hz, 2H), 4.20 (dd, $J = 11.4$, 2.6 Hz, 2H), 4.05 (s, 3H), 3.93–3.56 (m, 3H), 2.51–2.23 (m, 2H), 1.91 (dd, $J = 13.4$, 1.5 Hz, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 166.9, 163.9, 141.0, 140.9, 136.3, 130.4, 127.7, 124.6, 122.9, 68.3, 52.8, 39.4, 32.0.

HRMS (ES+) m/z calc. for C$_{16}$H$_{17}$NO$_3$Na [M+Na] 294.1106, found 294.1111.

FT-IR (cm$^{-1}$, neat, ATR) 2962, 1589, 1489, 1387, 850.

Methyl 1-(1-Tosylpiperidin-4-yl)isoquinoline-3-carboxylate (2d)

Physical state: 84 mg, 66% yield, pale yellow solid (mp = dec $\sim$195 $^\circ$C).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.42 (s, 1H), 8.11 (d, $J = 8.5$ Hz, 1H), 7.97 (d, $J = 8.0$ Hz, 1H), 7.74–7.66 (m, 4H), 7.37 (d, $J = 8.0$ Hz, 2H), 4.03 (s, 3H), 3.98 (d, $J = 11.5$ Hz, 2H), 3.53-3.48 (m, 1H), 2.62-2.52 (m, 2H), 2.48 (s, 3H), 2.45-2.32 (m, 2H), 2.05-2.03 (m, 2H).
$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.5, 162.9, 143.3, 140.6, 133.3, 130.2, 129.5, 129.2, 129.1(9), 128.8, 127.8, 127.4, 124.1, 122.8, 52.6, 46.3, 39.1, 30.4, 21.5.

HRMS (ES+) m/z calc. for C$_{23}$H$_{23}$N$_2$O$_4$S [M+H] 425.1535, found 425.1531.

FT-IR (cm$^{-1}$, neat, ATR) 2962, 1589, 1489, 1387, 850.

Methyl 1-((tert-Butoxycarbonyl)piperidin-4-yl)isoquinoline-3-carboxylate (2e)

Physical state: 41 mg, 51% yield, white semi-solid.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.42 (s, 1H), 8.25 (d, $J$ = 7.3 Hz, 1H), 8.06 – 7.89 (m, 1H), 7.84 – 7.64 (m, 2H), 4.32 (m, 2H), 4.02 (s, 3H), 3.72 (t, $J$ = 11.4 Hz, 1H), 2.99 (m, 2H), 2.03 (m, 4H), 1.49 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.8, 164.1, 154.9, 140.8, 136.3, 130.5, 129.4, 127.8, 124.6, 122.9, 79.6, 58.5, 52.8, 40.2, 31.2, 28.7.

HRMS (ES+) m/z calc. for C$_{21}$H$_{27}$N$_2$O$_4$ [M+H] 371.1971, found 371.1984.

FT-IR (cm$^{-1}$, neat, ATR) 2962, 1589, 1489, 1387, 850.

Methyl 1-((1-Hydroxy-3-phenylpropan-2-yl)isoquinoline-3-carboxylate (2f)

Physical state: 20 mg, 20% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.48 (s, 1H), 8.13 (d, $J$ = 8.4 Hz, 1H), 7.98 (d, $J$ = 8.1 Hz, 1H), 7.78 – 7.75 (m, 1H), 7.72 – 7.68 (m, 1H), 7.34 – 7.18 (m, 5H), 5.65 (d, $J$ = 10.1 Hz, 1H), 4.19 (d, $J$ = 11.3 Hz, 1H), 4.05 (s, 3H), 3.98 – 3.93 (m, 1H), 3.88 – 3.84 (m, 1H), 3.39 – 3.34 (m, 1H), 3.12 – 3.07 (m, 1H).
$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.2, 165.4, 140.1, 139.6, 136.3, 131.1, 129.9, 129.5, 129.4, 128.7, 128.0, 126.5, 125.0, 123.2, 63.1, 53.0, 44.4, 38.1.

**HRMS (ES+) m/z calc. for C$_{20}$H$_{20}$NO$_2$ [M+H] 322.1443, found 322.1452.**

**FT-IR (cm$^{-1}$, neat, ATR) 1734, 1451, 1244, 1207, 749, 702.**

![Chemical Structure](image)

Methyl 1-(Tetrahydrofuran-3-yl)isoquinoline-3-carboxylate (2g)

Physical state: 43.7 mg, 34% yield, colorless oil.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.45 (s, 1H), 8.27 (d, $J$ = 7.2 Hz, 1H), 8.00 – 7.93 (m, 1H), 7.80 – 7.70 (m, 2H), 4.42 – 4.32 (m, 2H), 4.25 – 4.15 (m, 2H), 4.08 – 3.96 (m, 4H), 2.79 – 2.57 (m, 1H), 2.53 – 2.31 (m, 1H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.5, 161.2, 136.0, 134.0, 130.4, 129.4, 129.0, 128.4, 124.8, 123.0, 112.7, 77.2, 68.8, 52.6, 43.4, 32.1.

**HRMS (ES+) m/z calc. for C$_{15}$H$_{16}$NO$_3$ [M+H] 258.1130, found 258.1140.**

**FT-IR (cm$^{-1}$, neat, ATR) 2987, 2870, 1208, 1063, 861, 837.**

![Chemical Structure](image)

Methyl 1-(1-(tert-Butoxycarbonyl)azetidin-3-yl)isoquinoline-3-carboxylate (2i)

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.50 (s, 1H), 8.01 (d, $J$ = 8.1 Hz, 1H), 7.89 (d, $J$ = 8.2 Hz, 1H), 7.82 – 7.71 (m, 2H), 4.64 – 4.45 (m, 5H), 4.05 (s, 3H), 1.47 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.3, 159.7, 156.3, 140.3, 135.9, 130.7, 129.7, 129.2, 127.7, 124.3, 123.4, 79.4, 52.6, 33.0, 28.3.

**HRMS (ES+) m/z calc. for C$_{19}$H$_{23}$N$_2$O$_4$ [M+H] 343.1658, found 343.1666.**
FT-IR (cm\(^{-1}\), neat, ATR) 2987, 2870, 1208, 1063, 861, 837.

Methyl 1-Cyclopropylishoquinoline-3-carboxylate (2j)

Physical state: 21 mg, 31% yield, clear oil.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.54 – 8.44 (m, 1H), 8.36 (s, 1H), 8.01 – 7.89 (m, 1H), 7.76 – 7.73 (m, 2H), 4.01 (s, 3H), 2.75 (tt, \(J = 8.5, 4.9\) Hz, 1H), 1.37 – 1.34 (m, 2H), 1.17 – 1.13 (m, 2H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 166.9, 162.5, 140.7, 135.8, 130.6, 129.5, 129.4, 129.0, 125.6, 122.3, 52.9, 14.4, 9.3.

HRMS (ES\(^+\)) m/z calc. for C\(_{14}\)H\(_{13}\)NO\(_2\) [M+H] 228.1025, found 228.1019.

FT-IR (cm\(^{-1}\), neat, ATR) 2951, 1737, 1321, 1269, 1244, 988.

Methyl 1-((3r,5r,7r)-Adamantan-1-yl)isoquinoline-3-carboxylate (2k)

Physical state: 43.4 mg, 45% yield, off-white solid (mp = 210–212 °C)

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 11.63 (s, 1H), 8.73 – 8.71 (m, 1H), 8.58 – 8.38 (m, 1H), 7.71 – 7.70 (m, 2H), 4.08 (s, 3H), 2.38 (s, 6H), 2.21 (s, 3H), 1.89 (m, 6H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 171.6, 157.4, 155.1, 129.5, 129.1, 128.6, 128.4, 126.8, 124.2, 118.5, 52.7, 42.2, 41.9, 37.0, 29.1.

HRMS (ES\(^+\)) m/z calc. for C\(_{21}\)H\(_{24}\)NO\(_2\) [M+H] 322.1807, found 322.1797.

FT-IR (cm\(^{-1}\), neat, ATR) 2951, 1737, 1321, 1269, 1244, 988.
Methyl 1-((1-Pyridin-2-yl)piperidin-4-yl)isoquinoline-3-carboxylate (21)

**Physical state:** 75 mg, 72% yield, yellow solid (mp = 154–157 °C).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.42 (s, 1H), 8.31 (s, 1H), 8.20 (s, 1H) 7.98 (d, $J = 3.5$ Hz, 1H), 7.76 – 7.74 (m, 2H), 7.49 – 7.45 (m, 1H), 6.74 (d, $J = 8.5$ Hz, 1H), 6.60-6.59 (m, 1H), 4.52 (d, $J = 12.5$ Hz, 2H), 4.00 (s, 3H), 3.82-3.80 (m, 1H), 3.12 (t, $J = 12.5$ Hz, 2H), 2.34-2.26 (m, 2H), 2.10-2.04 (m, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 166.9, 164.3, 159.6, 148.1, 140.9, 137.5, 136.3, 130.4, 129.4, 129.4, 127.8, 124.8, 122.9, 112.8, 107.4, 52.8, 45.8, 40.7, 31.2.

HRMS (ES+) m/z calc. for C$_{21}$H$_{22}$N$_3$O$_2$ [M+H] 348.1712, found 348.1714.

FT-IR (cm$^{-1}$, neat, ATR) 2962, 1589, 1489, 1387, 850.

**TERTIARY EXAMPLES**

1,3,9-Trimethyl-8-(2-methyl-1-phenylpropan-2-yl)-3,9-dihydro-1H-purine-2,6-dione (1v)

**Physical state:** 52 mg, 53% yield, pale yellow solid (mp = 101–103 °C).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.23-7.21 (m, 3H), 6.88-6.85 (m, 2H), 3.80 (s, 3H), 3.56 (s, 3H), 3.41 (s, 3H), 3.03 (s, 2H), 1.51 (s, 6H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 158.7, 155.5, 146.9(4), 146.9(1), 137.4, 129.8, 128.1, 126.7, 107.7, 48.2, 39.4, 33.8, 29.5, 27.8, 27.2.

HRMS (ES+) m/z calc. for C$_{17}$H$_{23}$N$_4$O$_2$ [M+H] 327.1821, found 327.1820.
FT-IR (cm⁻¹, neat, ATR) 3055, 2987, 1758, 1699, 1656, 1422, 1040, 896, 733, 703.

[Structural diagram]

2-(2-Methyl-1-phenylpropan-2-yl)benzo[d]thiazole (1w)

**Physical state:** 52 mg, 53% yield, pale yellow oil.

**¹H NMR** (500 MHz, CDCl₃) δ 8.05 (d, J = 8.2 Hz, 1H), 7.86 (dd, J = 8.0, 0.5 Hz, 1H), 7.53 – 7.44 (m, 1H), 7.41 – 7.32 (m, 1H), 7.27 – 7.12 (m, 3H), 7.09 – 6.98 (m, 2H), 3.18 (s, 2H), 1.52 (s, 6H).

**¹³C NMR** (126 MHz, CDCl₃) δ 180.7, 153.2, 137.6, 134.8, 130.4, 127.8, 126.3, 125.7, 124.5, 122.7, 121.4, 49.5, 42.2, 28.0.

**HRMS (ES⁺)** m/z calc. for C₁₇H₁₅NS [M+H] 268.1160, found 268.1168.

FT-IR (cm⁻¹, neat, ATR) 3028, 2927, 1505, 1495, 1385, 1280, 1005, 743, 687.

**PRIMARY ALKYLTRIFLUOROBORATE COUPLING**

[Structural diagram]

Methyl 1-((Cyclopentyloxy)methyl)isoquinoline-3-carboxylate (3a)

**Physical state:** 72 mg, 84% yield, clear viscous oil.

**¹H NMR** (500 MHz, CDCl₃) δ 8.52 (s, 1H), 8.45 (d, J = 7.7 Hz, 1H), 7.94 (d, J = 7.4 Hz, 1H), 7.74 (s, 2H), 5.10 (s, 2H), 4.13 (s, 1H), 4.04 (s, 3H), 1.52 (m, 8H).

**¹³C NMR** (126 MHz, CDCl₃) δ 166.5, 158.6, 140.3, 136.3, 130.9, 129.6, 129.1, 128.6, 126.7, 124.7, 82.3, 77.4, 77.2, 76.9, 72.5, 53.0, 32.4, 23.6.

**HRMS (ES⁺)** m/z calc. for C₁₇H₂₀NO₃ [M+H] 286.1443, found 286.1454.

FT-IR (cm⁻¹, neat, ATR) 2952, 1737, 1334, 1246, 1110, 1096, 791.
Methyl 1-((2-(Trimethylsilyl)ethoxy)methyl)isoquinoline-3-carboxylate (3b)

**Physical state:** 61 mg, 86% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.53 (s, 1H), 8.47 (d, $J = 7.9$ Hz, 1H), 7.96 (d, $J = 7.9$ Hz, 1H), 7.78 – 7.71 (m, 2H), 5.13 (s, 2H), 4.04 (s, 3H), 3.76 – 3.55 (m, 2H), 1.11 – 0.90 (m, 2H), -0.03 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.5, 158.4, 140.4, 136.3, 130.9, 129.6, 129.0, 128.6, 126.6, 124.7, 73.5, 68.5, 52.9, 18.5, -1.3.

HRMS (ES+) m/z calc. for C$_{17}$H$_{23}$NO$_3$Si [M+Na] 340.1345, found 340.1347.

FT-IR (cm$^{-1}$, neat, ATR) 2951, 1740, 1719, 1247, 1208, 860.

Methyl 1-(((3-Methylbut-3-en-1-yl)oxy)methyl)isoquinoline-3-carboxylate (3c)

**Physical state:** 55 mg, 64% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.54 (s, 1H), 8.49 (d, $J = 8.2$ Hz, 1H), 7.96 (d, $J = 7.9$ Hz, 1H), 7.78 – 7.70 (m, 2H), 5.16 (s, 2H), 4.74 (s, 1H), 4.70 (s, 1H), 4.04 (s, 3H), 3.68 (t, $J = 6.9$ Hz, 2H), 2.32 (t, $J = 6.9$ Hz, 2H), 1.68 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.4, 158.2, 142.8, 140.3, 136.3, 131.0, 129.6, 129.0, 128.6, 126.6, 124.8, 111.7, 74.2, 69.4, 53.0, 37.9, 22.7.

HRMS (ES+) m/z calc. for C$_{17}$H$_{25}$NO$_3$Na [M+Na] 308.1263, found 308.1263.

FT-IR (cm$^{-1}$, neat, ATR) 2950, 1738, 1450, 1295, 1209, 1109.
Methyl 1-(((1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl)oxy)methylisoquinoline-3-carboxylate (3d)

**Physical state:** 65 mg, 61% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.53 (s, 1H), 8.46 (d, $J = 7.7$ Hz, 1H), 7.95 (d, $J = 8.2$ Hz, 1H), 7.79 – 7.70 (m, 2H), 5.30 (d, $J = 11.3$ Hz, 1H), 5.04 (d, $J = 11.3$ Hz, 1H), 4.04 (s, 3H), 3.28 (td, $J = 10.5$, 4.1 Hz, 1H), 2.07 – 2.03 (m, 1H), 1.67 – 1.54 (m, 2H), 1.43 – 1.17 (m, 3H), 0.97 – 0.75 (m, 9H), 0.43 (d, $J = 6.9$ Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.6, 158.9, 140.3, 136.3, 130.9, 129.4, 129.2, 128.6, 127.0, 124.8, 79.3, 71.3, 52.9, 48.5, 40.4, 34.6, 31.6, 25.3, 23.1, 22.5, 21.1, 15.7.

HRMS (ES+) m/z calc. for C$_{22}$H$_{29}$NO$_3$Na [M+Na] 378.2047, found 378.2045.

FT-IR (cm$^{-1}$, neat, ATR) 2954, 2869, 1722, 1244, 1108, 984, 907, 688, 646.

Methyl 1-((3-(Benzyloxy)propyl)isoquinoline-3-carboxylate (3e)

**Physical state:** 52 mg, 56% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.45 (s, 1H), 8.21 (d, $J = 8.3$ Hz, 1H), 8.03 (d, $J = 7.4$ Hz, 2H), 7.96 (d, $J = 8.1$ Hz, 1H), 7.74 (t, $J = 7.5$ Hz, 1H), 7.68 (t, $J = 7.6$ Hz, 1H), 7.54 (t, $J = 7.0$ Hz, 1H), 7.42 (t, $J = 7.6$ Hz, 2H), 4.41 (t, $J = 6.4$ Hz, 2H), 4.04 (s, 3H), 3.46 (t, $J = 7.9$ Hz, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.8, 166.8, 162.5, 140.8, 136.1, 133.0, 133.0, 130.7, 130.6, 129.7, 129.7, 129.52, 129.1, 128.5, 125.6, 123.1, 100.1, 77.4, 77.2, 76.9, 64.9, 64.8, 62.6, 53.0, 35.3, 29.4, 29.0, 26.4, 25.4.

HRMS (ES+) m/z calc. for C$_{19}$H$_{17}$NO$_3$ [M+Na] 308.1287, found 308.1283.
Methyl 1-Isobutylisoquinoline-3-carboxylate (3f)

**Physical state:** 45 mg, 62% yield, clear oil.

$^1H$ NMR (500 MHz, CDCl$_3$) δ 8.43 (s, 1H), 8.21 (d, $J = 8.0$ Hz, 1H), 7.94 (d, $J = 7.8$ Hz, 1H), 7.71 (m, 2H), 4.03 (s, 3H), 3.25 (d, $J = 7.3$ Hz, 2H), 2.32 (m, 1H), 0.98 (d, $J = 6.7$ Hz, 6H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.9, 162.5, 140.8, 136.1, 130.5, 129.2, 129.0, 129.0, 125.9, 122.8, 52.9, 44.1, 29.8, 22.9.

HRMS (ES+) m/z calc. for C$_{15}$H$_{17}$NO$_2$Na [M+Na]$^+$ 266.1157, found 266.1161.

$^{1}H$ NMR (500 MHz, CDCl$_3$) δ 8.51 (s, 1H), 8.16 (d, $J = 8.4$ Hz, 1H), 7.95 (d, $J = 8.1$ Hz, 1H), 7.73 – 7.68 (m, 1H), 7.64 – 7.60 (m, 1H), 7.27 – 7.20 (m, 4H), 7.19 – 7.13 (t, $J = 7.0$ Hz, 1H), 4.78 (s, 2H), 4.07 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.7, 160.9, 140.8, 139.2, 136.4, 130.7, 129.6, 129.0, 128.8, 128.7 128.7, 126.5, 126.4, 123.7, 53.0, 42.6.

HRMS (ES+) m/z calc. for C$_{18}$H$_{16}$NO$_2$ [M+H]$^+$ 278.1181, found 278.1171.

$^{1}H$ NMR (500 MHz, CDCl$_3$) δ 8.51 (s, 1H), 8.16 (d, $J = 8.4$ Hz, 1H), 7.95 (d, $J = 8.1$ Hz, 1H), 7.73 – 7.68 (m, 1H), 7.64 – 7.60 (m, 1H), 7.27 – 7.20 (m, 4H), 7.19 – 7.13 (t, $J = 7.0$ Hz, 1H), 4.78 (s, 2H), 4.07 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.7, 160.9, 140.8, 139.2, 136.4, 130.7, 129.6, 129.0, 128.8, 128.7 128.7, 126.5, 126.4, 123.7, 53.0, 42.6.

HRMS (ES+) m/z calc. for C$_{18}$H$_{16}$NO$_2$ [M+H]$^+$ 278.1181, found 278.1171.
Methyl 1-Phenethylisoquinoline-3-carboxylate (3h)

**Physical state:** 28 mg, 32% yield, clear oil.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 8.47\) (s, 1H), 8.19 (d, \(J = 8.2\) Hz, 1H), 7.96 (d, \(J = 7.9\) Hz, 1H), 7.78 – 7.66 (m, 2H), 7.32 – 7.15 (m, 5H), 4.06 (s, 3H), 3.76 – 3.62 (m, 2H), 3.28 – 3.15 (m, 2H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta 166.8, 166.8, 162.0, 141.8, 140.8, 136.1, 130.7, 129.5, 129.1, 128.6, 128.6, 126.2, 125.5, 123.2, 53.0, 37.4, 35.6 (one aryl carbon peak overlaps).

HRMS (ES+) m/z calc. for C\(_{19}\)H\(_{18}\)NO\(_2\) [M+H] 314.1157, found 314.1157.

FT-IR (cm\(^{-1}\), neat, ATR) 2949, 1737, 1716, 1240, 1208, 749.

Methyl 1-(3-Phenylpropyl)isoquinoline-3-carboxylate (3i)

**Physical state:** 76% yield, clear oil.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 8.44\) (s, 1H), 8.06 (d, \(J = 8.3\) Hz, 1H), 7.94 (d, \(J = 8.0\) Hz, 1H), 7.76 – 7.68 (m, 2H), 7.35 – 7.26 (m, 2H), 7.25 – 7.16 (m, 3H), 4.05 (s, 3H), 3.48 – 3.27 (m, 2H), 2.81 (t, \(J = 7.7\) Hz, 2H), 2.26 – 2.19 (m, 2H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta 166.8, 162.8, 142.1, 140.8, 136.1, 130.6 129.4, 129.0, 128.7, 128.5, 128.5, 126.0, 125.6, 123.1, 53.0, 36.1, 35.2, 31.6.

HRMS (ES+) m/z calc. for C\(_{20}\)H\(_{20}\)NO\(_2\) [M+H] 306.1494, found 306.1492.

FT-IR (cm\(^{-1}\), neat, ATR) 2949, 1736, 1716, 1242, 1209, 747.
Methyl 1-(4-(2-Bromophenyl)butyl)isoquinoline-3-carboxylate (3j)

**Physical state:** 67 mg, 56% yield, clear oil.

**$^1$H NMR** (500 MHz, CDCl$_3$) $\delta$ 8.44 (s, 1H), 8.20 (d, $J = 8.0$ Hz, 1H), 7.95 (d, $J = 7.8$ Hz, 1H), 7.75 – 7.70 (m, 2H), 7.51 (d, $J = 8.0$ Hz, 1H), 7.24 – 7.19 (m, 2H), 7.03 (s, 1H), 4.04 (s, 3H), 3.42 (t, $J = 8.1$ Hz, 2H), 2.85 – 2.76 (m, 2H), 2.01 – 1.90 (m, 2H), 1.85 – 1.76 (m, 2H).

**$^{13}$C NMR** (126 MHz, CDCl$_3$) $\delta$ 166.8, 162.9, 141.7, 140.8, 136.1, 132.9, 130.6, 130.5, 129.4, 129.0, 128.5, 127.6, 125.7, 123.0, 53.0, 36.2, 35.7, 30.2, 29.8.

**HRMS (ES+) m/z calc.** for C$_{21}$H$_{20}$BrNO$_2$ [M+Na] 420.0575, found 420.0576.

**FT-IR (cm$^{-1}$, neat, ATR)** 2946, 1735, 1438, 1239, 1207, 1020, 748.

Methyl 1-(3-(Phenylthio)propyl)isoquinoline-3-carboxylate (3k)

**Physical state:** 50 mg, 49% yield, clear oil.

**$^1$H NMR** (500 MHz, CDCl$_3$) $\delta$ 8.44 (s, 1H), 8.15 (d, $J = 8.4$ Hz, 1H), 7.95 (d, $J = 8.1$ Hz, 1H), 7.76 – 7.70 (m, 1H), 7.70 – 7.64 (m, 1H), 7.36 (d, $J = 7.7$ Hz, 2H), 7.31 – 7.21 (m, 2H), 7.19 – 7.14 (m, 1H), 4.04 (s, 3H), 3.58 – 3.46 (m, 2H), 3.11 (t, $J = 7.0$ Hz, 2H), 2.30 – 2.21 (m, 2H).

**$^{13}$C NMR** (126 MHz, CDCl$_3$) $\delta$ 166.7, 161.9, 140.7, 136.5, 136.1, 130.7, 129.6, 129.4, 129.0, 128.5, 126.1 125.6, 123.2, 53.0, 34.4, 33.6, 29.0 (one aryl peak overlaps).

**HRMS (ES+) m/z calc.** for C$_{20}$H$_{20}$NO$_2$S [M+H] 338.1215, found 338.1198.

**FT-IR (cm$^{-1}$, neat, ATR)** 2950, 1735, 1438, 1325, 1294, 1243, 1210.
Methyl 1-(3,3,3-Trifluoropropyl)isoquinoline-3-carboxylate (3l)

**Physical state:** 15 mg, 18% yield, viscous oil.

\[^1^H\text{NMR}\] (500 MHz, CDCl\(_3\)) \(\delta\) 8.48 (s, 1H), 8.20 (d, \(J = 8.6\) Hz, 1H), 8.06 – 7.93 (m, 1H), 7.86 – 7.74 (m, 2H), 4.05 (s, 3H), 3.68 – 3.57 (m, 2H), 2.96 – 2.77 (m, 2H).

\[^{13}C\text{NMR}\] (126 MHz, CDCl\(_3\)) \(\delta\) 166.5, 158.7, 140.6, 136.0, 131.1, 130.1, 129.3, 128.4, 124.8, 123.7, 53.1, 32.5 (q, \(J = 29.0\) Hz), 29.0, 27.4.

\[^{19}F\text{NMR}\] (471 MHz, CDCl\(_3\)) \(\delta\) -66.42.

**HRMS (ES+)** m/z calc. for C\(_{14}\)H\(_{12}\)F\(_3\)NO\(_2\Na\) [M+Na] 306.0718, found 306.0721.

**FT-IR** (cm\(^{-1}\), neat, ATR) 3071, 1715, 1240, 1126.

Methyl 1-(But-3-en-1-yl)isoquinoline-3-carboxylate (3p)

**Physical state:** 40 mg, 55% yield, crystalline powder (mp = 54–57 °C).

\[^1^H\text{NMR}\] (500 MHz, CDCl\(_3\)) \(\delta\) 8.44 (s, 1H), 8.21 (d, \(J = 7.9\) Hz, 1H), 7.95 (d, \(J = 7.9\) Hz, 1H), 7.76 – 7.68 (m, 2H), 6.05 – 5.90 (m, 1H), 5.12 (d, \(J = 17.0\) Hz, 1H), 5.01 (d, \(J = 10.2\) Hz, 1H), 4.04 (s, 3H), 3.47 (t, \(J = 8.2\) Hz, 2H), 2.70 – 2.60 (m, 2H).

\[^{13}C\text{NMR}\] (126 MHz, CDCl\(_3\)) \(\delta\) 166.7, 162.3, 140.8, 137.8, 136.1, 130.6, 129.5, 129.1, 128.5, 125.6, 123.1, 115.3, 53.0, 35.0, 33.8.

**HRMS (ES+)** m/z calc. for C\(_{15}\)H\(_{15}\)NO\(_2\Na\) [M+Na] 264.1000, found 264.0998.

**FT-IR** (cm\(^{-1}\), neat, ATR) 1748, 1656, 1596, 1157.
DIVERSITY TABLE

4-Methyl-2-((2-(Trimethylsilyl)ethoxy)methyl)quinoline (4a)


Physical state: 62 mg, 77% yield, clear oil.

\[^1H\] NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 8.05 (d, \(J = 8.4\) Hz, 1H), 7.98 (d, \(J = 8.3\) Hz, 1H), 7.71 – 7.66 (m, 1H), 7.55 – 7.51 (m, 1H), 7.46 (s, 1H), 4.74 (s, 2H), 3.72 – 3.63 (m, 2H), 2.71 (s, 3H), 1.11 – 1.03 (m, 2H), -0.03 (s, 9H).

\[^{13}C\] NMR (126 MHz, CDCl\textsubscript{3}) \(\delta\) 159.3, 147.5, 145.0, 129.7, 129.3, 127.7, 126.1, 123.8, 120.2, 74.1, 68.6, 19.0, 18.5, -1.2.

FT-IR (cm\textsuperscript{-1}, neat, ATR) 2953, 1603, 1249, 1101, 850, 836, 757.

1-(4-Methylquinolin-2-yl)-3-phenylpropyl benzoate (4b)

Physical state: 48 mg, 42% yield, clear oil.

\[^1H\] NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 8.15 (d, \(J = 7.7\) Hz, 2H), 8.10 (d, \(J = 8.4\) Hz, 1H), 7.97 (d, \(J = 8.3\) Hz, 1H), 7.72 – 7.69 (m, 1H), 7.62 – 7.59 (m, 1H), 7.56 – 7.52 (m, 1H), 7.51 – 7.47 (m, 2H), 7.34 (s, 1H), 7.30 – 7.12 (m, 5H), 6.20 (dd, \(J = 8.3, 5.1\) Hz, 1H), 2.90 – 2.78 (m, 2H), 2.69 (s, 3H), 2.60 – 2.45 (m, 2H).

\[^{13}C\] NMR (126 MHz, CDCl\textsubscript{3}) \(\delta\) 166.1, 159.7, 147.6, 145.3, 141.5 133.3, 130.3, 130.0, 129.4, 128.8, 128.6, 128.4, 127.8, 126.5, 126.4, 126.1, 123.8, 119.1, 36.9, 32.1, 19.1.

HRMS (ES+) m/z calc. for C\textsubscript{36}H\textsubscript{23}NO\textsubscript{2} [M+Na] 404.1626, found 404.1630.

FT-IR (cm\textsuperscript{-1}, neat, ATR) 1719, 1602, 1451, 1270, 1111, 1070, 1027, 713.
2-((But-3-en-1-yloxy)methyl)quinoline (4e)

**Physical state:** 24 mg, 38% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.18 (d, $J = 8.4$ Hz, 1H), 8.05 (d, $J = 8.7$ Hz, 1H), 7.82 (d, $J = 8.4$ Hz, 1H), 7.72 – 7.68 (m, 1H), 7.64 – 7.61 (m, 1H), 7.54 – 7.51 (m, 1H), 5.92 – 5.84 (m, 1H), 5.15 – 5.06 (m, 2H), 4.82 (s, 2H), 3.65 (t, $J = 6.6$ Hz, 2H), 2.45 (m, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 159.6, 147.7, 136.9, 135.3, 129.7, 129.1, 127.8, 127.7, 126.4, 119.5, 116.7, 74.6, 70.5, 34.4.

HRMS (ES+) m/z calc. for C$_{14}$H$_{16}$NO [M+H] 214.1232, found 214.1234.

FT-IR (cm$^{-1}$, neat, ATR) 2858, 1601, 1506, 1428, 1359, 1106, 996, 916, 829, 784, 755, 618.

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2-Octylquinoline (4d)

**Physical state:** 32 mg, 44% yield, yellow oil.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.80 (d, $J = 4.4$ Hz, 1H), 8.11 (d, $J = 8.4$ Hz, 1H), 8.04 (d, $J = 8.4$ Hz, 1H), 7.71 – 7.68 (m, 1H), 7.57 – 7.54 (m, 1H), 7.23 (d, $J = 4.3$ Hz, 1H), 3.09 – 3.04 (m, 2H), 1.80 – 1.73 (m, 2H), 1.47 – 1.41 (m, 2H), 1.40 – 1.17 (m, 8H), 0.88 (t, $J = 6.6$ Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 150.4, 148.9, 148.5, 130.4, 129.1, 127.8, 126.3, 123.8, 120.9, 32.3, 32.0, 30.3, 29.9, 29.6, 29.4, 22.8, 14.2.

HRMS (ES+) m/z calc. for C$_{17}$H$_{24}$N [M+H] 242.1909, found 242.1904.

FT-IR (cm$^{-1}$, neat, ATR) 2924, 2855, 1592, 1508, 1463, 760.

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2-((2R)-2-Methylcyclopentyl)quinoline (4e)
**Physical state:** 38 mg, 60% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.08 – 8.04 (m, 2H), 7.77 (d, $J = 8.1$ Hz, 1H), 7.69 – 7.65 (m, 1H), 7.49 – 7.45 (m, 1H), 7.31 (d, $J = 8.6$ Hz, 1H), 2.90 – 2.84 (m, 1H), 2.33 – 2.17 (m, 2H), 2.09 – 1.93 (m, 2H), 1.92 – 1.77 (m, 2H), 1.45 – 1.37 (m, 1H), 1.01 (d, $J = 6.5$ Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 165.6, 148.1, 136.2, 129.3, 129.2, 127.6, 127.1, 125.7, 120.4, 57.3, 42.5, 35.2, 34.3, 24.5, 19.0.

HRMS (ES+) m/z calc. for C$_{15}$H$_{18}$N [M+H] 212.1439, found 212.1444.

FT-IR (cm$^{-1}$, neat, ATR) 3050, 2946, 1601, 1255.

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1,1'-((3-Phenethylpyridine-2,6-diyl)bis(ethan-1-one) (4f)

**Physical state:** 52 mg, 65% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.04 (d, $J = 8.0$ Hz, 1H), 7.62 (d, $J = 8.0$ Hz, 1H), 7.30 – 7.25 (m, 2H), 7.22 – 7.18 (m, 3H), 3.33 – 3.30 (m, 2H), 2.93 – 2.90 (m, 2H), 2.75 (s, 3H), 2.73 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 201.8, 199.4, 151.1, 150.6, 142.0, 141.0, 140.9, 128.8, 128.6, 126.4, 123.7, 37.4, 35.4, 28.4, 25.7.

HRMS (ES+) m/z calc. for C$_{17}$H$_{18}$NO$_2$ [M+H] 268.1338, found 268.1339.

FT-IR (cm$^{-1}$, neat, ATR) 1699, 1358, 1296, 700.

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2-(1-(Benzyloxy)-2-phenylethyl)benzo[\(d\)]thiazole (4g)

**Physical state:** 52 mg, 53% yield, colorless oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.07 – 8.00 (m, 1H), 7.92 (d, $J = 8.0$ Hz, 1H), 7.52 – 7.47 (m, 1H), 7.43 – 7.36 (m, 5H), 7.35 – 7.31 (m, 1H), 7.28 – 7.24 (m, 2H), 7.17 (d, $J = 7.8$ Hz, 3H), 4.85 (dd, $J = 8.3$, 4.8 Hz, 1H), 4.70 (d, $J = 11.4$ Hz, 1H), 4.52 (d, $J = 11.4$ Hz, 1H), 2.93 – 2.82 (m, 1H), 2.82 – 2.71 (m, 1H), 2.41 – 2.29 (m, 1H), 2.29 – 2.19 (m, 2H).
$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 175.4, 153.3, 141.3, 137.6, 135.1, 128.7, 128.6(5), 128.5(7), 128.3, 128.1, 126.1(5), 126.1(3), 125.3, 123.2, 122.1, 79.0, 72.3, 38.9, 31.7.

HRMS (ES+) m/z calc. for C$_{23}$H$_{23}$NOS [M+H] 360.1422, found 360.1420.

FT-IR (cm$^{-1}$, neat, ATR) 3027, 2922, 2861, 1516, 1495, 1093, 1027, 1014, 758, 697.

3-Isopropyl-1H-indazole (4h)

Physical state: 33 mg, 69% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.84 (bs, 1H), 7.78 (d, $J = 8.1$ Hz, 1H), 7.45 – 7.42 (m, 1H), 7.38 – 7.35 (m, 1H), 7.15 – 7.12 (m, 1H), 3.44 (sept, $J = 7.0$ Hz, 1H), 1.48 (d, $J = 7.0$ Hz, 6H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 152.8, 141.6, 126.7, 126.7, 121.4, 120.8, 120.2, 109.9, 27.9, 22.3.

HRMS (ES+) m/z calc. for C$_{10}$H$_{12}$N$_2$ [M+] 160.1000, found 160.1001.

FT-IR (cm$^{-1}$, neat, ATR) 3189, 2968, 1623, 1501, 1349, 742.

2-Isopropylquinazolin-4(3H)-one (4i)


Physical state: 45 mg, 79% yield, white solid (mp = 123 °C).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 11.64 (s, 1H), 8.30 (d, $J = 7.9$ Hz, 1H), 7.79 – 7.72 (m, 2H), 7.47 – 7.45 (m, 1H), 3.06 (sept, $J = 7.0$ Hz, 1H), 1.45 (d, $J = 7.0$ Hz, 6H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 164.4, 161.0, 149.6, 134.8, 127.5, 126.4, 126.4, 120.9, 35.1, 20.6.

HRMS (ES+) m/z calc. for C$_{11}$H$_{12}$N$_2$ONa [M+Na] 211.0847, found 211.0851.

FT-IR (cm$^{-1}$, neat, ATR) 2970, 2932, 1622, 1609, 1472, 1384, 1252, 772.
2-((1R,2R)-2-Methylcyclohexyl)quinazolin-4(3H)-one (4j)

**Physical state:** 30 mg, 41% yield, white powder (mp = 89–93 °C).

\[ \text{H NMR (500 MHz, CDCl}_3\text{)} \delta 11.48 (s, 1H), 8.29 (d, J = 7.9 Hz, 1H), 7.80 – 7.71 (m, 2H), 7.48 – 7.46 (m, 1H), 2.39 – 2.33 (m, 1H), 2.05 – 1.96 (m, 2H), 1.92 – 1.73 (m, 4H), 1.57 – 1.49 (m, 1H), 1.43 – 1.35 (m, 1H), 1.26 – 1.12 (m, 1H), 0.88 (d, J = 6.5 Hz, 3H). \]

\[ \text{C NMR (126 MHz, CDCl}_3\text{)} \delta 164.1, 159.9, 149.6, 134.8, 127.5, 126.4, 120.9, 100.1, 52.9, 35.2, 35.2, 31.5, 26.2, 26.1, 20.6. \]

\[ \text{HRMS (ES+) m/z calc. for C}_{15}\text{H}_{19}\text{N}_{2}\text{O} \text{[M+H]} 243.1497, \text{found 243.1500.} \]

\[ \text{FT-IR (cm}^{-1}, \text{ neat, ATR) 2926, 1668, 1471, 773.} \]

1,3,7-Trimethyl-8-((2S)-2-methylcyclopentyl)-3,7-dihydro-1H-purine-2,6-dione (4k)

**Physical state:** 31 mg, 37%, light yellow oil.

\[ \text{H NMR (500 MHz, CDCl}_3\text{)} \delta 3.93 (s, 3H), 3.56 (s, 3H), 3.40 (s, 3H), 2.67 – 2.63 (m, 1H), 2.50 – 2.40 (m, 1H), 2.14 – 2.01 (m, 2H), 1.96 – 1.76 (m, 4H), 1.02 (d, J = 6.5 Hz, 3H). \]

\[ \text{C NMR (126 MHz, CDCl}_3\text{)} \delta 157.6, 155.5, 152.0, 148.4, 107.4, 148.4, 41.3, 34.6, 32.4, 31.7, 29.9, 28.0, 24.2, 19.2. \]

\[ \text{HRMS (ES+) m/z calc. for C}_{14}\text{H}_{21}\text{N}_{4}\text{O}_{2} \text{[M+H]} 277.1658, \text{found 277.1661.} \]

\[ \text{FT-IR (cm}^{-1}, \text{ neat, ATR) 2954, 1703, 1661, 1543, 1436, 1221, 1041, 981, 747.} \]
(1R)-(2-Isopropyl-6-methoxyquinolin-4-yl)(5-vinylquinuclidin-2-yl)methanol (4I)

**Physical state:** 82 mg, 75% yield, light yellow solid (mp = 145 °C).

**1H NMR** (500 MHz, CDCl$_3$) $\delta$ 7.89 (d, $J$ = 9.1 Hz, 1H), 7.52 (s, 1H), 7.22 (d, $J$ = 9.1 Hz, 1H), 7.07 (s, 1H), 5.80 (s, 1H), 5.73 – 5.60 (m, 1H), 5.00 – 4.92 (m, 2H), 3.81 – 3.73 (m, 4H), 3.62 – 3.53 (m, 4H), 3.26 – 3.08 (m, 3H), 2.85 – 2.75 (m, 3H), 2.42 – 2.35 (m, 1H), 1.90 – 1.80 (m, 2H), 1.65 – 1.60 (m, 1H), 1.49 – 1.39 (m, 1H), 1.34 (d, $J$ = 6.9 Hz, 6H).

**13C NMR** (126 MHz, CDCl$_3$) $\delta$ 164.7, 157.6, 146.3, 143.8, 140.1, 131.3, 124.7, 121.5, 116.5, 115.8, 100.6, 60.2, 60.1, 56.2, 55.9, 43.7, 39.0, 37.2, 27.7, 26.4, 22.7, 20.2.

**HRMS (ES+)** m/z calc. for C$_{23}$H$_{30}$N$_2$O$_2$ [M+H] 367.2361, found 367.2394.

**FT-IR** (cm$^{-1}$, neat, ATR) 2962, 1674, 1620, 1236.

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**LIGAND FUNCTIONALIZATION**

2,9-Di-tert-butyl-1,10-phenanthroline (5b)


**Physical state:** 38 mg, 42% yield, white semi-solid.

**1H NMR** (500 MHz, CDCl$_3$) $\delta$ 8.13 (d, $J$ = 8.4 Hz, 2H), 7.84 – 7.48 (m, 4H), 1.60 (s, 18H).

**13C NMR** (126 MHz, CDCl$_3$) $\delta$ 169.4, 157.6, 145.0, 136.0, 127.0, 125.5, 119.7, 38.8, 30.4.

**HRMS (ES+)** m/z calc. for C$_{20}$H$_{25}$N [M+H] 293.2018, found 293.2020.
2,9-Di-tert-butyl-4,7-diphenyl-1,10-phenanthroline (5d)


**Physical state**: 152 mg, 68% yield, yellow oil.

$^1$H NMR (500 MHz, CDCl$_3$) \( \delta \) 7.72 (s, 2H), 7.63 (s, 2H), 7.56 – 7.43 (m, 10H), 1.64 (s, 18H).

$^{13}$C NMR (126 MHz, CDCl$_3$) \( \delta \) 168.8, 148.4, 145.7, 139.2, 129.9, 128.6, 128.2, 124.9, 123.1, 120.1, 38.9, 30.5.

HRMS (ES+) m/z calc. for C$_{15}$H$_{16}$F$_2$N [M+H] 248.1251, found 248.1241.

FT-IR (cm$^{-1}$, neat, ATR) 2962, 1589, 1489, 1387, 850.

2-(tert-Butyl)-6-(2,4-difluorophenyl)pyridine (5f)

**Physical state**: 61 mg, 82% yield, light yellow oil.

$^1$H NMR (500 MHz, CDCl$_3$) \( \delta \) 8.61 (d, \( J = 5.1 \) Hz, 1H), 7.96 (m, 1H), 7.28 – 7.22 (m, 1H), 6.99 (t, \( J = 8.4 \) Hz, 1H), 6.91 (m, 1H), 1.36 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) \( \delta \) 163.2 (dd, \( J = 250.5, 12.1 \) Hz), 160.6 (dd, \( J = 252.0, 11.9 \) Hz), 160.6, 149.8, 132.4 (dd, \( J = 9.7, 4.6 \) Hz), 124.5 (dd, \( J = 12.0, 3.9 \) Hz), 122.6, 121.5 (d, \( J = 8.9 \) Hz), 119.7, 111.9 (dd, \( J = 21.0, 3.8 \) Hz), 104.4 (m), 35.0, 30.7.

HRMS (ES+) m/z calc. for C$_{13}$H$_{16}$F$_2$N [M+H] 248.1251, found 248.1241.

FT-IR (cm$^{-1}$, neat, ATR) 2949, 1736, 1716, 1242, 1209, 747, 700.
6-(tert-Butyl)-2,2':6',2''-terpyridine (5h)

**Physical state:** 64 mg, 74% yield, yellow oil.

**$^1$H NMR** (500 MHz, CDCl$_3$) δ 8.75 (s, 1H), 8.71 – 8.60 (m, 3H), 8.45 (m, 2H), 7.94 (m, 1H), 7.86 (m, 1H), 7.33 (dt, $J=6.7, 3.5$ Hz, 2H), 1.43 (s, 9H).

**$^{13}$C NMR** (126 MHz, CDCl$_3$) δ 160.9, 156.3, 155.6, 149.3, 149.3, 138.1, 137.0, 137.0, 123.9, 121.3, 121.1, 121.1, 120.9, 118.2, 35.1, 30.7.

**HRMS (ES+) m/z** calc. for: submitted.

**FT-IR** (cm$^{-1}$, neat, ATR) 2963, 1602, 1579, 1548, 1456, 1391, 820, 770.

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HETEROARENE WITH FUNCTION HANDLES

4-((Benzyloxy)methyl)-5-bromopyrimidine (6a)

**Physical state:** 42 mg, 50% yield, clear oil.

**$^1$H NMR** (500 MHz, CDCl$_3$) δ 9.13 (s, 1H), 8.77 (s, 1H), 7.43 – 7.30 (m, 5H), 4.73 (s, 2H), 4.71 (s, 2H).

**$^{13}$C NMR** (126 MHz, CDCl$_3$) δ 164.1, 158.9, 157.1, 137.4, 128.7, 128.2, 120.3, 73.7, 71.1.

**HRMS (ES+) m/z** calc. for C$_{12}$H$_{12}$BrN$_3$O [M+H] 279.0133, found 279.0135.

**FT-IR** (cm$^{-1}$, neat, ATR) 2860, 1560, 1454, 1388, 1360, 1216, 1097, 1036, 738, 698.
3-Bromo-4-methyl-2-(1-tosylpiperidin-4-yl)pyridine and 5-bromo-4-methyl-2-(1-tosylpiperidin-4-yl)pyridine (6b)

Physical state: 69 mg, 57% yield, white amorphous solid (mp = 120–122 °C).

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.52 (s, 1H – minor isomer), 8.31 (d, $J = 4.8$ Hz, 1H – major isomer), 7.72 – 7.67 (m, 3H – both isomers), 7.38 – 7.33 (m, 2H – both isomers), 7.01 (d, $J = 4.8$ Hz, 1H – major isomer), 6.99 (s, 2H – minor isomer), 3.94 (m, 2H – both isomers), 3.16 (m, 1H – both isomers), 2.61 – 2.34 (m, 8H – both isomers), 2.12 – 1.79 (m, 4H – both isomers).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 161.0, 147.6, 147.1, 129.5, 127.7, 127.6, 123.9, 122.9, 121.6, 46.3, 41.6, 29.7, 23.4, 21.4. (major peaks)

HRMS (ES+) m/z calc. for C$_{18}$H$_{22}$BrN$_2$O$_2$S [M+H] 408.0585, found 409.0586.

FT-IR (cm$^{-1}$, neat, ATR) 3052, 2915, 2801, 1351, 1331, 1160, 927, 726, 648, 548.

3-Bromo-4-methyl-2-phenethylpyridine (6c)

Physical state: 50 mg, 60% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.33 (d, $J = 4.8$ Hz, 1H), 7.30 (d, $J = 4.4$ Hz, 4H), 7.21 (p, $J = 4.1$ Hz, 1H), 7.03 (d, $J = 4.8$ Hz, 1H), 3.37 – 3.22 (m, 2H), 3.05 (dd, $J = 10.2$, 6.7 Hz, 2H), 2.43 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 159.9, 147.9, 147.2, 141.9, 128.6, 128.5, 126.1, 124.3, 123.9, 40.4, 34.8, 23.6.

HRMS (ES+) m/z calc. for C$_{14}$H$_{14}$BrN [M+H] 276.0388, found 276.0388.

FT-IR (cm$^{-1}$, neat, ATR) 1727, 1591, 1435, 1281, 1258, 1084, 738, 698.
4-Chloro-2-phenethylquinoline (6d)

**Physical state:** 38 mg, 47% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.20 (d, $J$ = 8.3 Hz, 1H), 8.08 (d, $J$ = 8.4 Hz, 1H), 7.76 (t, $J$ = 7.7 Hz, 1H), 7.60 (t, $J$ = 7.6 Hz, 1H), 7.35 (s, 1H), 7.30 (t, $J$ = 7.5 Hz, 2H), 7.22 (dd, $J$ = 15.9, 8.7 Hz, 2H), 3.29 – 3.23 (m, 2H), 3.16 (dd, $J$ = 9.7, 6.3 Hz, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 161.9, 149.0, 142.7, 141.3, 130.5, 129.4, 128.6, 126.9, 126.3, 125.2, 124.1, 121.7, 40.9, 35.8.

HRMS (ES+) m/z calc. for C$_{17}$H$_{15}$ClN [M+H] 268.0893, found 268.0896.

FT-IR (cm$^{-1}$, neat, ATR) 3062, 3027, 1589, 1493, 1149, 866, 759, 698.

4-Bromo-3-isopropylisoquinoline (6e)

**Physical state:** 30 mg, 40% yield, clear oil.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.67 (s, 1H), 8.24 – 8.18 (m, 2H), 7.79 – 7.76 (m, 1H), 7.67 – 7.64 (m, 1H), 3.91 (sept, $J$ = 6.8 Hz, 1H), 1.43 (d, $J$ = 6.8 Hz, 6H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 166.1, 143.8, 135.0, 130.9, 127.9, 127.7, 127.0, 125.2, 117.7, 31.2, 22.3.

HRMS (ES+) m/z calc. for C$_{12}$H$_{13}$BrN [M+H] 250.0231, found 250.0224.

FT-IR (cm$^{-1}$, neat, ATR) 2965, 2929, 1565, 1387, 1240, 1009, 928.
4-Bromo-1-isopropylisoquinoline (6f)

**Physical state:** 22 mg, 29% yield, clear oil.

**1H NMR** (500 MHz, CDCl₃) δ 8.51 (s, 1H), 8.35 (d, J = 8.5 Hz, 1H), 7.62 – 7.59 (m, 1H), 7.52 – 7.49 (m, 1H), 7.43 (d, J = 8.5 Hz, 1H), 4.08 (sept, J = 6.8 Hz, 1H), 1.55 (d, J = 6.8 Hz, 6H).

**13C NMR** (126 MHz, CDCl₃) δ 166.8, 143.2, 136.3, 129.9, 127.1, 126.9, 126.3, 125.9, 125.1, 31.3, 22.4.

**HRMS (ES+)** m/z calc. for C₁₂H₁₄BrN [M+H] 250.0231, found 250.0224.

**FT-IR** (cm⁻¹, neat, ATR) 2965, 1556, 1502, 1388, 1246, 765.

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**CAMPTOTHECIN ANALOGUES**

![Chemical structure of (S)-4-Ethyl-4-hydroxy-11-isopropyl-1,12-dihydro-14H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H)-dione (7a)](image)

(S)-4-Ethyl-4-hydroxy-11-isopropyl-1,12-dihydro-14H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H)-dione (7a)


**Physical state:** 67 mg, 57% yield, light yellow solid (mp = 192 °C).

**1H NMR** (500 MHz, CDCl₃) δ 8.25 – 8.20 (m, 2H), 7.79 – 7.76 (m, 1H), 7.70 – 7.61 (m, 2H), 5.74 (d, J = 16.1 Hz, 1H), 5.38 (s, 2H), 5.30 (d, J = 16.1 Hz, 1H), 4.05 – 3.92 (m, 1H), 3.90 (bs, 1H), 1.94 – 1.84 (m, 2H), 1.56 (d, J = 8.3 Hz, 6H), 1.03 (t, J = 7.4 Hz, 3H).

**13C NMR** (126 MHz, CDCl₃) δ 174.1, 157.7, 152.5, 150.4, 149.9, 149.5, 146.6, 130.9, 130.1, 127.8, 126.9, 125.5, 123.9, 118.5, 98.0, 72.9, 66.5, 50.4, 31.8, 21.7, 21.6, 8.0.

**HRMS (ES+)** m/z calc. for C₂₃H₂₂N₂O₄ [M+Na] 413.1477, found 413.1460.

**FT-IR** (cm⁻¹, neat, ATR) 3320, 2971, 1748, 1657, 1157, 727.
(S)-11-((Benzyloxy)methyl)-4-ethyl-4-hydroxy-1,12-dihydro-14H-pyranol[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H)-dione (7b)

**Physical state:** 23 mg, 33% yield, yellow oil.

**1H NMR** (500 MHz, CDCl₃) δ 8.22 (d, J = 8.5 Hz, 1H), 7.96 (d, J = 8.5 Hz, 1H), 7.80 - 7.76 (m, 1H), 7.69 - 7.59 (m, 2H), 7.42 – 7.34 (m, 5H), 5.75 (d, J = 16.2 Hz, 1H), 5.42 (s, 2H), 5.31 (d, J = 16.2 Hz, 1H), 5.18 (s, 2H), 4.78 (s, 2H), 3.78 (s, 1H), 1.95 – 1.86 (m, 2H), 1.04 (t, J = 7.4 Hz, 3H).

**13C NMR** (126 MHz, CDCl₃) δ 174.1, 157.8, 152.8, 150.1, 149.1, 146.5, 139.4, 137.1, 130.7, 130.3, 128.9, 128.5, 128.1, 128.1, 127.2, 126.0, 123.5, 118.8, 97.9, 73.9, 72.9, 67.2, 66.6, 51.0, 31.8, 8.0.

**HRMS (ES+)** m/z calc. for C₂₈H₂₅N₂O₅ [M+H] 469.1763, found 469.1774.

**FT-IR** (cm⁻¹, neat, ATR) 2987, 2870, 1208, 1063, 861, 837.

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**SYNTHESIS OF TERTIARY ALKYLTRIFLUOROBORATE**

Potassium Trifluoro(2-methyl-1-phenylpropan-2-yl)borate (1u)


**1H NMR** (500 MHz, acetone-d₆) δ 7.16 – 7.13 (m, 2H), 7.08 – 7.05 (m, 3H), 2.52 (s, 2H), 0.63 (s, 6H). Peaks at 0.75 and 0.13 correspond to EtBF₃K generated during borylation procedure.

**13C NMR** (126 MHz, acetone-d₆) δ 142.1, 130.5, 126.6, 124.2, 44.5, 22.5 (carbon α to boron not observed due to quadrupolar relaxation).

**19F NMR** (470.7 MHz, acetone-d₆) δ -153.1 (product), -142.7 (EtBF₃K).
**11B NMR** (128.4 MHz, acetone-\text{d}_6) \( \delta -6.43 \).

**HRMS (ES+)** \( m/z \) calc. for C\(_{10}\)H\(_{13}\)BF\(_3^-\) [M-] calc. 201.0198, found: submitted.

**FT-IR** (cm\(^{-1}\), neat, ATR) 2970, 2928, 2861, 1467, 1225, 1019, 945, 749, 702.

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**CYCLIC VOLTAMMETRY OF ORGANOBORON REAGENTS**

Electrochemical measurements were recorded on a CH Instruments: Model 600E Series Electrochemical Analyzer (observed in 0.002 M MeCN; \([\text{N(Bu)}_4]PF_6\) = 0.1 M; Ag/AgCl = electrode; reported in SCE based on a ferrocene internal standard).

![Graph showing t-BuBF\(_3\)K Oxidation Potential vs Voltage (V) vs SCE.]

Of the organoboron reagents examined, only the potassium cyclohexyltriolborate \( XX \) (~1.1 V vs SCE) and potassium cyclohexyltrifluoroborate (~1.5 V vs SCE) exhibited oxidations within the solvent window of MeCN. These potentials have been reported previously by Akita and coworkers (*Adv. Synth. Cat.* 2012, 354 (18), 3414). No features were observed for oxidation of the cyclohexyl boronic acid, MIDA, and pincaol boronates.
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-(tert-butyl)quinoline (1a)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-(tert-butyl)quinoline (1a)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-(tert-butyl)-4-methylquinoline (1b)

JKM-04-095-1.1.fid
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-(tert-butyl)-4-methylquinoline (1b)

JKM-04-095-1_13C.1.fid
$^1$H (CDCl$_3$, 500 MHz) spectra of 4-bromo-2-(tert-butyl)quinoline (1c)

JKM-04-097-1.1.fid
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 4-bromo-2-(tert-butyl)quinoline (1c)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-(tert-butyl)-4-chloro-8-(trifluoromethyl)quinoline (1d)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-((tert-butyl)-4-chloro-8-(trifluoromethyl)quinoline (1d)

JKM-03-206_chloroCF3quinoline_13C.1.fid
$^1$H (CDCl$_3$, 500 MHz) spectra of 3-(tert-butyl)-1H-indazole (1e)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 3-(tert-butyl)-1H-indazole (1e)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(tert-butyl)isouquinoline-3-carboxylate (1g)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-((tert-butyl)isoquinoline-3-carboxylate (1g)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-(tert-butyl)quinoxaline (1h)
\(^{13}\)C NMR (CDCl\(_3\), 125.8 MHz) spectrum of 2-(\textit{tert}-butyl)quinoxaline (1h)

JKM-03-206_quinoxaline_13C.1.fid
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-(tert-butyl)-3-chloroquinoxaline (1i)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-((tert-butyl)-3-chloroquinoxaline (II)}
$^1$H (CDCl$_3$, 500 MHz) spectra of 6-(tert-butyl)nicotinonitrile (1j)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 6-(tert-butyl)nicotinonitrile (1j)
$^{19}$F (CDCl$_3$, 477 MHz) spectra of 2-(tert-Butyl)-4-(trifluoromethyl)pyridine (Ik) with fluorobenzene

Product peak

3 equiv of fluorobenzene (internal standard)
\( ^1H (\text{CDCl}_3, 500 \text{ MHz}) \) spectra of 1,1\'-\((4\text{-}\text{tert-buty}l)\text{pyridine-2,6-diyl})\text{bis(ethan-1-one)} \) (11)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 1,1'-(4-(tert-butyl)pyridine-2,6-diyl)bis(ethan-1-one) (11)
$^1$H (CDCl$_3$, 500 MHz) spectra of 8-(tert-butyl)-1,3,7-trimethyl-3,7-dihydro-1H-purine-2,6-dione (1m)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 8-(tert-butyl)-1,3,7-trimethyl-3,7-dihydro-1H-purine-2,6-dione (1m)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-(tert-butyl)nicotinamide (1n)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-(tert-butyl)nicotinamide (1n)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-(tert-butyl)benzo[d]thiazole (1o)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-(tert-butyl)benzo[d]thiazole (10)

JKM-03-234_benzothiazole_13C.1.fid
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-(tert-butyl)quinazolin-4(3H)-one (1p)
\[^1^3\]C NMR (CDCl\textsubscript{3}, 125.8 MHz) spectrum of 2-(\textit{tert}-butyl)quinazolin-4(3\textit{H})-one (1p)
$^1$H (CDCl$_3$, 500 MHz) spectra of $N$-benzyl-2-(tert-butyl)-7H-purin-6-amine (1q)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of $N$-benzyl-2-(tert-butyl)-7H-purin-6-amine (1q)
$^1$H (CDCl$_3$, 500 MHz) spectra of (1R)-(2-(tert-butyl)-6-methoxyquinolin-4-yl)(5-vinylquinuclidin-2-yl)methanol (1r)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of (1R)-(2-((tert-butyl)-6-methoxyquinolin-4-yl)(5-vinylquinuclidin-2-yl)methanol (1r)

JKM-03-222_quinuine_13C.1.fid
$^1$H (CDCl$_3$, 500 MHz) spectra of 1,3,9-trimethyl-8-(2-methyl-1-phenylpropan-2-yl)-3,9-dihydro-1H-purine-2,6-dione (1v)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 1,3,9-trimethyl-8-(2-methyl-1-phenylpropan-2-yl)-3,9-dihydro-1H-purine-2,6-dione (1v)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-(2-methyl-1-phenylpropan-2-yl)benzo[d]thiazole (1w)
$^{13}$C NMR (CDCl₃, 125.8 MHz) spectrum of 2-(2-methyl-1-phenylpropan-2-yl)benzo[d]thiazole (1w)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(1-(benzyl oxy)-3-phenylpropyl)isoquinoline-3-carboxylate (2a)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(1-(benzyloxy)-3-phenylpropyl)isoquinoline-3-carboxylate (2a)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(4,4-difluorocyclohexyl)isoquinoline-3-carboxylate (2b)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(4,4-difluorocyclohexyl)isoquinoline-3-carboxylate (2b)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(tetrahydro-2H-pyran-4-yl)isoquinoline-3-carboxylate (2c)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(tetrahydro-2H-pyran-4-yl)isoquinoline-3-carboxylate (2e)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(1-tosylpiperidin-4-yl)isoquinoline-3-carboxylate (2d)
$^{13}$C (CDCl$_3$, 125.8 MHz) spectra of methyl 1-(1-tosylpiperidin-4-y1)isoquinoline-3-carboxylate (2d)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-((tert-butoxycarbonyl)piperidin-4-yl)isoquinoline-3-carboxylate (2e)
$^{13}$C (CDCl₃, 125.8 MHz) spectra of methyl 1-[(tert-butoxycarbonyl)piperidin-4-yl]isoquinoline-3-carboxylate (2e)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(1-hydroxy-3-phenylpropan-2-yl)isoquinoline-3-carboxylate (2f)

![Chemical structure of methyl 1-(1-hydroxy-3-phenylpropan-2-yl)isoquinoline-3-carboxylate (2f)]
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(1-hydroxy-3-phenylpropan-2-yl)isoquinoline-3-carboxylate (2f)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of methyl 1-(tetrahydrofuran-3-yl)isoquinoline-3-carboxylate (2g)
$^1$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(tetrahydrofuran-3-yl)isoquinoline-3-carboxylate (2g)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of methyl 1-(1-(tert-butoxycarbonyl)azetidin-3-yl)isoquinoline-3-carboxylate (2i)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(1-(tert-butoxycarbonyl)azetidin-3-yl)isoquinoline-3-carboxylate (2i)
$^1$H (CDCl₃, 500 MHz) spectra of methyl 1-cyclopropylisoquinoline-3-carboxylate (2j)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-cyclopropylisoquinoline-3-carboxylate (2j)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-((3r,5r,7r)-adamantan-1-yl)isoquinoline-3-carboxylate (2k)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-((3$r$,5$r$,7$r$)-adamantan-1-yl)isoquinoline-3-carboxylate (2k)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(1-(pyridin-2-yl)piperidin-4-yl)isoquinoline-3-carboxylate (2I)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(1-(pyridin-2-yl)piperidin-4-yl)isoquinoline-3-carboxylate (21)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-((cyclopentyloxy)methyl)isoquinoline-3-carboxylate (3a)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-((cyclopentyloxy)methyl)isoquinoline-3-carboxylate (3a)

![Chemical Structure](image)

**1H NMR**

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<th>198.81</th>
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<th>201.50</th>
<th>201.51</th>
<th>201.52</th>
</tr>
</thead>
</table>

S97
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-((2-(trimethylsilyl)ethoxy)methyl)isoquinoline-3-carboxylate (3b)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-((2-(trimethylsilyl)ethoxy)methyl)isoquinoline-3-carboxylate (3b)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(((3-methylbut-3-en-1-yl)oxy)methyl)isoquinoline-3-carboxylate (3c)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(((3-methylbut-3-en-1-yl)oxy)ethyl)isoquinoline-3-carboxylate (3c)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)methyl)isoquinoline-3-carboxylate (3d)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-((((1$R$,2$S$,5$R$)-2-isopropyl-5-methylcyclohexyl)oxy)methyl)isoquinoline-3-carboxylate (3d)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(3-(benzyloxy)propyl)isoquinoline-3-carboxylate (3e)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-((3-(benzzyloxy)propyl)isoquinoline-3-carboxylate (3e)

JKM-04-010-4_13C.1.fid

![S105 Image]
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-isobutylisoquinoline-3-carboxylate (3f)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-isobutylisoquinoline-3-carboxylate (3f)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-benzylisoquinoline-3-carboxylate (3g)
\(^{13}\)C NMR (CDCl\(_3\), 125.8 MHz) spectrum of methyl 1-benzylisoquinoline-3-carboxylate (3g)

![C NMR spectrum of methyl 1-benzylisoquinoline-3-carboxylate (3g)](attachment:13C_NMR_spectrum.png)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-phenethylisoquinoline-3-carboxylate (3h)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-phenyleisoquinoline-3-carboxylate (3h)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(3-phenylpropyl)isoquinoline-3-carboxylate (3i)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(3-phenylpropyl)isoquinoline-3-carboxylate (3i)

JKM-04-102_13C.1.fid

S113
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(4-(2-bromophenyl)butyl)isoquinoline-3-carboxylate (3j)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(4-(2-bromophenyl)butyl)isoquinoline-3-carboxylate (3j)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(3-(phenylthio)propyl)isoquinoline-3-carboxylate (3k)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(3-(phenylthio)propyl)isoquinoline-3-carboxylate ($3k$)
$^1$H (CDCl$_3$, 500 MHz) spectra of methyl 1-(3,3,3-trifluoropropyl)isoquinoline-3-carboxylate (31)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(3,3,3-trifluoropropyl)isoquinoline-3-carboxylate (3l)
\[^1\text{H} (\text{CDCl}_3, 500 \text{ MHz})\] spectra of methyl 1-(but-3-en-1-yl)isoquinoline-3-carboxylate (3p)

JKM-04-028-1.1.fid

[Chemical structure diagram]
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of methyl 1-(but-3-en-1-yl)isoquinoline-3-carboxylate (3p)
$^1$H (CDCl$_3$, 500 MHz) spectra of 4-methyl-2-((2-(trimethylsilyl)ethoxy)methyl)quinoline (4a)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 4-methyl-2-((2-(trimethylsilyl)ethoxy)methyl)quinoline (4a)
$^1$H (CDCl$_3$, 500 MHz) spectra of 1-(4-methylquinolin-2-yl)-3-phenylpropyl benzoate (4b)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 1-(4-methylquinolin-2-yl)-3-phenylpropyl benzoate (4b)

![Chemical structure of the compound](attachment:JKM-03-260_benzoate_13C.1.fid)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-((but-3-en-1-ylxy)methyl)quinoline (3c)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-((but-3-en-1-yloxy)methyl)quinoline (3e)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-octylquinoline (3d)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-((2R)-2-methylcyclopentyl)quinoline (3e)

JKM-03-226_methylcyclopentyl 1.1.fid
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-((2R)-2-methycyclopentyl)quinoline (3e)

![Chemical Structure Diagram]
$^1$H (CDCl$_3$, 500 MHz) spectra of 1,1'-(3-phenethylpyridine-2,6-diyl)bis(ethan-1-one) (3f)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 1,1'-((3-phenethylpyridine-2,6-diy)bis(ethan-1-one) (3f)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-(1-(benzyloxy)-2-phenylethyl)benzo[d]thiazole (3g)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-((1-(benzyloxy)-2-phenylethyl)benzo[d]thiazole (3g)
$^1$H (CDCl$_3$, 500 MHz) spectra of 3-Isopropyl-1H-indazole (3h)

1H NMR

![NMR Spectrum](image)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 3-isopropyl-1H-indazole (3h)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-isopropylquinazolin-4(3H)-one (3i)

JKM-03-248_4-hydroxyquinazoline.1.fid
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-isopropylquinazolin-4(3H)-one (3i)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-((1$R$,2$R$)-2-methylecyclohexyl)quinazolin-4(3$H$)-one (3)}
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-((1R,2R)-2-methylcyclohexyl)quinazolin-4(3H)-one (3j)
$^1$H (CDCl$_3$, 500 MHz) spectra of 1,3,7-trimethyl-8-((2S)-2-methylcyclopentyl)-3,7-dihydro-1$H$-purine-2,6-dione (3k)

JKM-03-228_methyl cyclopropyl1.fid

![Chemical Structure](image-url)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 1,3,7-trimethyl-8-((2S)-2-methylcyclopentyl)-3,7-dihydro-1H-purine-2,6-dione (3k)
$^1$H (CDCl$_3$, 500 MHz) spectra of (1R)-(2-isopropyl-6-methoxyquinolin-4-yl)(5-vinylquinuclidin-2-yl)methanol (41)

S144
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of (1$R$)-(2-isopropyl-6-methoxyquinolin-4-yl)(5-vinylquinuclidin-2-yl)methanol (41)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2,9-di-tert-butyl-1,10-phenanthroline (5b)

JKM-03-202phenanthrolene.1.fid
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2,9-di-tert-butyl-1,10-phenanthroline ($5b$)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2,9-di-tert-butyl-4,7-diphenyl-1,10-phenanthroline (5d)

JKM-04-097-2.1.fid
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2,9-di-tert-butyl-4,7-diphenyl-1,10-phenanthroline (5d)
$^1$H (CDCl$_3$, 500 MHz) spectra of 2-$(\text{tert}-\text{butyl})$-6-$(2,4$-difluorophenyl)pyridine (5f)

JKM-04-095-3.1.fid
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 2-($\text{tert}$-butyl)-6-(2,4-difluorophenyl)pyridine (5f)
$^{1}$H (CDCl$_3$, 500 MHz) spectra of 6-(tert-butyl)-2,2':6',2"-terpyridine (5h)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 6-(tert-butyl)-2,2':6',2''-terpyridine (5h)

DNP-IV-terpy-ammonium.2.fid

S153
$^1$H (CDCl$_3$, 500 MHz) spectra of 4-((benzyloxy)methyl)-5-bromopyrimidine (6a)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 4-((benzyloxy)methyl)-5-bromopyrimidine (6a)

![Chemical Structure](image)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum 3-bromo-4-methyl-2-(1-tosylpiperidin-4-yl)pyridine and 5-bromo-4-methyl-2-(1-tosylpiperidin-4-yl)pyridine (6b)

ratio $= \sim 3.53 : 1$
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 3-bromo-4-methyl-2-(1-tosylpiperidin-4-yl)pyridine and 5-bromo-4-methyl-2-(1-tosylpiperidin-4-yl)pyridine (6b)

ratio $\approx 3.53 : 1$
$^1$H (CDCl$_3$, 500 MHz) spectra of 3-bromo-4-methyl-2-phenethylpyridine (6c)

JKM-04-042-3.1.fid
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 3-bromo-4-methyl-2-phenethylpyridine (6c)

JKM-04-042-3_13C.1.fid
\(^1\)H (CDCl\(_3\), 500 MHz) spectra of 4-chloro-2-phenethylquinoline (6d)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 4-chloro-2-phenethylquinoline (6d)

![Carbon-13 NMR spectrum of 4-chloro-2-phenethylquinoline (6d)]
$^1$H (CDCl$_3$, 500 MHz) spectra of 4-bromo-3-isopropylisoquinoline (6e)

![Chemical structure image]
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 4-bromo-3-isopropylisoquinoline (6e)
\(^1\)H (CDCl\(_3\), 500 MHz) spectra of 4-bromo-1-isopropylisoquinoline (6f)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of 4-bromo-1-isopropylisoquinoline (6f)

JKM-03-276_4-bromoisoquinolines_13C.1.fid
$^1$H (CDCl$_3$, 500 MHz) spectra of \((S)-4$-ethyl-4-hydroxy-11-isopropyl-1,12-dihydro-14$H$-pyrano[3',4':6,7]indolizino[1,2-$b$]quinoline-3,14(4$H$)-dione (7a)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of (S)-4-ethyl-4-hydroxy-11-isopropyl-1,12-dihydro-14$H$-pyrano[3',4':6,7]indolizino[1,2-$b$]quinoline-3,14(4$H$)-dione (7a)
\(^1\)H (CDCl\(_3\), 500 MHz) spectra of (S)-11-((benzylloxy)methyl)-4-ethyl-4-hydroxy-1,12-dihydro-14\(H\)-pyrano[3',4':6,7]indolizino[1,2-\(b\)]quinoline-3,14(4\(H\))-dione (7b)
$^{13}$C NMR (CDCl$_3$, 125.8 MHz) spectrum of (S)-11-((benzylxy)methyl)-4-ethyl-4-hydroxy-1,12-dihydro-14H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H)-dione (7b)
$^1$H NMR (acetone-d$_6$, 500 MHz) spectrum of Potassium trifluoro(2-methyl-1-phenylpropan-2-yl)borate (1u)
$^{13}$C NMR (acetone-$d_6$, 125.8 MHz) spectrum of Potassium trifluoro(2-methyl-1-phenylpropan-2-yl)borate (1u)
$^{19}$F NMR (acetone-d$_6$, 470.7 MHz) spectrum of Potassium trifluoro(2-methyl-1-phenylpropan-2-yl)borate (1u)
$^{11}$B NMR (acetone-d$_6$, 128.4 MHz) spectrum of Potassium trifluoro(2-methyl-1-phenylpropan-2-yl)borate (1u)
$^1$H NMR (CD$_3$CN, 500 MHz) spectrum of quinoline

![quinoline spectrum](image)
$^1$H NMR (CD$_3$CN, 500 MHz) spectrum of quinoline + TFA

JKM-04-quinoline studies-2.1.fid
$^1$H NMR

\[ \begin{align*}
  &\text{quinoline} + \text{TFA} \\
  &\text{H}_2\text{O}
\end{align*} \]
$^1$H NMR (CD$_3$CN, 500 MHz) spectrum of quinoline + BF$_3$
1H NMR (CD$_3$CN, 500 MHz) spectrum of quinoline + TFA + BF$_3$
$^{13}$C NMR (CD$_3$CN, 125.8 MHz) spectrum of quinoline
$^{13}$C NMR (CD$_3$CN, 125.8 MHz) spectrum of quinoline + TFA
$^{13}$C NMR (CD$_3$CN, 125.8 MHz) spectrum of quinoline + BF$_3$
$^{13}$C NMR (CD$_3$CN, 125.8 MHz) spectrum of quinoline + TFA + BF$_3$
Determination of Quantum Yield


\[
\phi = \frac{\text{mmol of product}}{(\text{photon flux})(t)(f)}
\]

The following reaction was used to determine quantum yield:

\[\text{t-BuBF}_3 + \begin{array}{c}
\text{MeAcr (5 mol %)} \\
\text{K}_2\text{S}_2\text{O}_8, \text{trifluoroacetic acid}
\end{array} \rightarrow \begin{array}{c}
\text{MeCN/H}_2\text{O (1:1)} \\
\text{monitored photon flux}
\end{array}\]

The absorbance of 9-mesityl-10-methylacridinium perchlorate was measured in MeCN/H$_2$O (1:1). Subsequently, the reaction (with remaining reagents) was irradiated at a wavelength where the photocatalyst absorbs and the $\phi_{\text{Fe}^{2+}}$ has been reported (reference: Demas, J. N.; Bowman, W. D.; Zalewski, E. F.; Velapoldl, R. A. *J. Phys. Chem.* **1981**, *85*, 2766). At 407 nm, the absorbance (A) was 0.71805:

\[f = 1 - 10^{-A}\]

\[f = 1 - 10^{0.71805} = 0.8086\]
The lights of the laboratory were shut off, and photocatalyst, heteroarene, persulfate, and MeCN/H$_2$O were added to the cuvette. Trifluoroacetic acid and trifluoroborate were added last and then the cuvette was capped with a PTFE stopper. Ar was bubbled through the reaction for 300 s, and under Ar, the sample was stirred and irradiated (406 nm, slit width = 10.0 cm) for 3600 s. After irradiation, the crude mixture was diluted with EtOAc and passed through a silica plug. The filtrate was concentrated. $^1$H NMR was used to determine the yield (3.16 x 10$^{-6}$ mol after 3600 s).

Standard ferrioxalate actinometry was used to determine the photon flux of the spectrophotometer. Potassium ferrioxalate hydrate was used to determine formation of Fe$^{2+}$ by observing formation of [Fe(phen)$_3$]$^{2+}$ after addition of 1,10-phenanthroline. A 0.15 M solution of ferrioxalate was prepared by dissolving 501 mg of potassium ferrioxalate hydrate in 6.8 mL of 0.05 M H$_2$SO$_4$, and this solution was stored in the dark. A buffered solution of phen was prepared by dissolving 11.1 mg phen and 2.5 g NaOAc in 11.1 mL of 0.5 M H$_2$SO$_4$, and this solution was also stored in the dark.

Absorbance of non-irradiated sample: A solution of phen (0.35 mL) was added to ferrioxalate solution (2.0 mL) in a vial that was covered with foil. The vial was capped and allowed to rest for 1 h before being transferred to a cuvette. The absorbance of the non-irradiated solution was measured to be 0.5875.

Absorbance of irradiated sample: The solution of ferrioxalate (2.0 mL) was stirred and irradiated for 90 s at 406 nm with a slit width of 10.0 nm. After irradiation, the buffered solution of phen (0.35 mL) was added to the cuvette and allowed to rest for 1 h in the dark. The absorbance was then found to be 2.3697.

Calculations:

$$\text{mol Fe}^{2+} = \frac{(V)(\Delta A)}{(1)(\varepsilon)} = \frac{(0.00235 \text{ L})(2.3607 - 0.58752)}{(1 \text{ cm})(11,110 \text{ mol}^{-1} \text{cm}^{-1})} = 3.751 \times 10^{-7}$$

$$\text{photon flux} = \frac{\text{mol Fe}^{2+}}{\phi(\text{Fe}^{2+})(t)(f)} = \frac{3.751 \times 10^{-7}}{(1.188)(90 \text{ s})(1.00)} = 3.508 \times 10^{-9} \text{ einstein/s}$$

$$\phi = \frac{\text{mmol of product}}{(\text{photon flux})(t)(f)} = \frac{3.160 \times 10^{-6} \text{ mol}}{(3.508 \times 10^{-9} \text{ s}^{-1})(3600 \text{ s})(0.8086)} = 0.31$$

The quantum yield supports a closed catalytic pathway.
BF₃ Studies with Alternate Radical Precursors

Reactions were performed on 0.1 mmol scale under standard conditions (containing 10% internal standard, 4,4'-di-tert-butylibiphenyl) where the alkylation partner was replaced by the respective sulfinate or carboxylic acid precursors. For the reactions with added BF₃, an etherate solution (48% by weight) was added to the reaction mixture after addition of all the other reagents. After 24 hours, the reaction was quenched by addition of equal volume of 1.0 M K₂CO₃. The resultant mixture was extracted 3 times with CH₂Cl₂. The aqueous layer was inspected by TLC to confirm full extraction. An aliquot of the CH₂Cl₂ layer was then placed on the GCMS, and the ratio of C2/C4 alkylation was determined by integration.

Comparison to other radical precursors

1:1 mixture with 1 equiv BF₃K
no reaction with 1 equiv sulfinate
no reaction with 1 equiv sulfinate and 1 equiv BF₃

1:1 mixture with 1 equiv acid
1:1 mixture with 1 equiv acid and 1 equiv BF₃
8:1 mixture with 1 equiv BF₃K
DFT Calculations: Radical Association with BF₃

Calculations were performed using: um06/6-311+G(d,p), smd:water //ub3lyp/6-31g(d) [ub3lyp/6-31g(d)].

![Diagram of radical association with BF₃](image)

- \( \text{BF}_3 \cdot \leftrightarrow \text{Et} \cdot + \text{BF}_3 \)
  - \( G_{\text{rel}} \): 3.6 [6.0]  
  - \( K_{\text{eq}} \): 4.6x10² [2.5x10⁴]

- \( \text{BF}_3 \cdot \leftrightarrow \text{iPr} \cdot + \text{BF}_3 \)
  - \( G_{\text{rel}} \): 3.2 [5.8]  
  - \( K_{\text{eq}} \): 2.1x10² [1.7x10⁴]

- \( \text{BF}_3 \cdot \leftrightarrow \text{tBu} \cdot + \text{BF}_3 \)
  - \( G_{\text{rel}} \): 2.5 [6.1]  
  - \( K_{\text{eq}} \): 0.7x10² [2.9x10⁴]

- \( \text{CO}_2\text{H} \cdot \leftrightarrow \text{tBu} \cdot + \text{CO}_2\text{H} \)
  - \( G_{\text{rel}} \): -10.1 [-36.1]  
  - \( K_{\text{eq}} \): 3.8x10⁻⁸ [3.6x10⁻²⁷]