

Supporting Information

A Sequential Au(I)/TBAF-Promoted Rapid and Selective Functionalization of Heteroarene N-Oxides with Alkynes

Mengfei Jiang,[†] Huilong Zhu,[†] Lei Huang, Du Luo, Heping Shi, Zhou Xu,^{*} Nan Wu^{*}

Jiangsu Key Laboratory of New Drug Research and Clinical Pharmacy, Xuzhou Medical University

^{*}Corresponding Author(s): xuzhou@xzhmu.edu.cn, wunan_china@163.com

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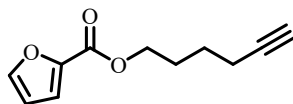
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1. General information

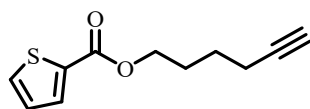
All reactions were carried out in air unless otherwise stated. For thin layer chromatography (TLC), Yantai pre-coated TLC plates (HSGF 254) were used, and compounds were visualized with a UV light at 254 nm. Column chromatography separations were performed on silica gel (300–400 mesh). Ethyl acetate and petroleum ether were used as eluents. NMR spectra were recorded on a JEOL ECZ400 400 MHz spectrometers (400 MHz for ^1H , 101 MHz for ^{13}C) with TMS as an internal standard and CDCl_3 as solvent. Chemical shifts were reported in δ (ppm) referenced to the residual solvent peak of CDCl_3 (δ 7.26) for ^1H NMR and CDCl_3 (δ 77.0) for ^{13}C NMR. Multiplicity abbreviated as: s, singlet; d, doublet; t, triplet; q, quartet; se-Pt, Septet; m, multiplet. Coupling constants were reported in Hertz (Hz). Fourier transform infrared spectra (FT-IR) were recorded on Agilent Technologies Cary 630 instrument. High resolution mass spectra (HRMS) were performed on Agilent G6550A Q-TOF (ESI). Melting points were measured on micro melting point apparatus and uncorrected. Unless otherwise noted, all commercialized reagents were used as received without further purification. Analytical grade solvents were used. The alkynes were prepared according to the known literature.

2. Characterization of alkynes

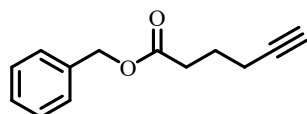
The alkynes were prepared according to the known literature.^[1-5]



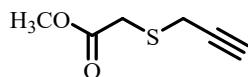
hex-5-yn-1-yl furan-2-carboxylate (21).^[1] Colorless liquid. (0.246 g, 64%, 2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.60 – 7.57 (m, 1H), 7.17 (d, J = 3.5 Hz, 1H), 6.50 (ddd, J = 3.5, 1.7, 0.7 Hz, 1H), 4.33 (t, J = 6.7 Hz, 2H), 2.27 (td, J = 6.6 Hz, 2.2 Hz, 2H), 1.96 (td, J = 2.6, 0.7 Hz, 1H), 1.92 – 1.85 (m, 2H), 1.67 (dt, J = 14.4, 7.2 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.9, 146.4, 144.9, 118.0, 111.9, 83.9, 68.9, 64.5, 27.9, 25.0, 18.2.



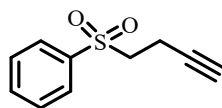
hex-5-yn-1-yl thiophene-2-carboxylate (2t).^[2] Colorless liquid. (0.354 g, 85%, 2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.80 (dd, $J = 3.7, 1.1$ Hz, 1H), 7.54 (dd, $J = 5.0, 1.1$ Hz, 1H), 7.10 (dd, $J = 4.9, 3.8$ Hz, 1H), 4.32 (t, $J = 6.4$ Hz, 2H), 2.27 (td, $J = 7.0, 2.6$ Hz, 2H), 1.97 (t, $J = 2.6$ Hz, 1H), 1.92 – 1.85 (m, 2H), 1.69 (p, $J = 7.1$ Hz, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 162.4, 134.0, 133.5, 132.4, 127.9, 84.0, 68.9, 64.7, 27.9, 25.1, 18.2.



benzyl hex-5-ynoate (2u).^[3] Colorless liquid. (0.316 g, 78%, 2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.31 (m, 5H), 5.13 (s, 2H), 2.51 (t, $J = 7.4$ Hz, 2H), 2.27 (td, $J = 6.9, 2.6$ Hz, 2H), 1.97 – 1.95 (m, 1H), 1.88 (p, $J = 7.2$ Hz, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 173.0, 136.1, 128.7, 128.4, 128.3, 83.4, 69.3, 66.4, 33.1, 23.7, 18.0.



methyl 2-(prop-2-yn-1-ylthio)acetate (Substrate of 6t).^[4] Colorless liquid. (0.150g, 52%, 2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 3.75 (s, 3H), 3.43 (s, 2H), 3.40 (d, $J = 2.6$ Hz, 2H), 2.28 (t, $J = 2.6$ Hz, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 170.6, 79.0, 72.0, 52.6, 32.5, 20.1.

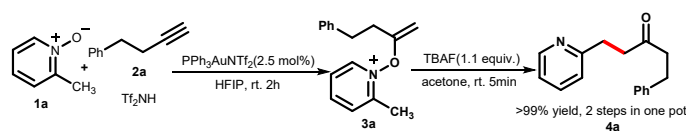


(but-3-yn-1-ylsulfonyl)benzene (Substrate of 6u).^[5] White solid. (0.291 g, 75%, 2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.92 (dd, $J = 8.3, 1.3$ Hz, 2H), 7.68 (t, $J = 7.4$ Hz, 1H), 7.59 (t, $J = 7.6$ Hz, 2H), 3.33 – 3.29 (m, 2H), 2.65 – 2.61 (m, 2H), 1.95 (t, $J = 2.7$ Hz, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 138.6, 134.2, 129.6, 128.4, 79.4, 70.7, 54.7, 13.4.

3. Optimization of reaction conditions using TBAF as a base reagent.

The reaction proved highly compatible with a sequential Au/TBAF catalytic system, as initial screening experiments showed (Table S1, entry 1). Inspired by the above result, we then investigated the F sources and solvents to potentially render this rearrangement reaction. First, we investigated the effect of different fluoride sources. Substituting TBAF with TMAF led to a slightly reduced yield of 87%, while using KF as the fluoride source gave a moderate yield of 71% (entries 2-3). A much lower yield of 30% was observed with $\text{NEt}_3 \cdot 3\text{HF}$ (entry 4), suggesting that $\text{NEt}_3 \cdot 3\text{HF}$ might not be a strong enough base or might not provide sufficient free fluoride ions for efficient reaction progression. Replacing TBAF with DIPEA or triethylamine reduced 4a yields to 65% and 81%, emphasizing TBAF's critical role in enhancing efficiency within the sequential Au/TBAF catalytic system (entries 5-6). Reducing the amount of TBAF to 0.4 equivalents resulted in a significantly lower yield (entry 7). However, the yield improved to >99% when the temperature was increased to 60°C, even with 0.4 equivalents of TBAF (entry 8). Further reducing the TBAF to 0.2 equivalents still produced a reasonable yield of 83%, though the reaction required 24 hours (entry 9). Finally, we examined the role of different solvents. Polar solvents like THF performed well but were slightly less efficient (entry 10), whereas HFIP and methanol significantly hindered the reaction, likely due to their polarity and potential interactions with TBAF (entries 11-12).

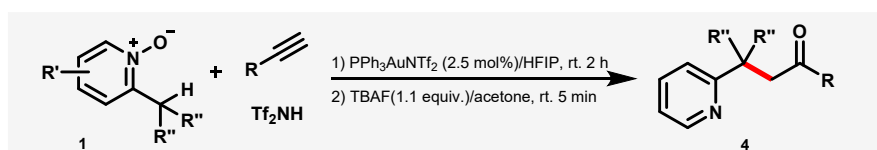
Table S1. Optimization of reaction conditions using TBAF as a base reagent.



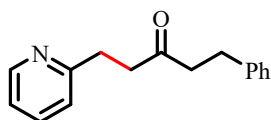
Entry	Deviation from the initially conditions	Yield
1	none	>99%
2	TMAF instead of TBAF, 5h	87%
3	KF instead of TBAF, 8h	71%
4	$\text{NEt}_3 \cdot 3\text{HF}$ instead of TBAF, 8h	30%
5	DIPEA instead of TBAF	65%
6	Et_3N instead of TBAF	81%
7	0.4 equiv. TBAF, rt, 12h	45%
8	0.4 equiv. TBAF, 60 °C, 10h	>99%
9	0.2 equiv. TBAF was used, 60 °C, 24h	83%
10	Same with entry 6, THF instead	90%
11	Same with entry 6, HFIP instead	16%
12	Same with entry 6, MeOH instead	45%

^a 0.12 mmol of **1a**, 0.1 mmol of **2a**, 0.11 mmol of Tf_2NH , 0.11 mmol of TBAF, solvent (0.5 mL). ^bYield determined by ^1H NMR by comparison with internal standard.

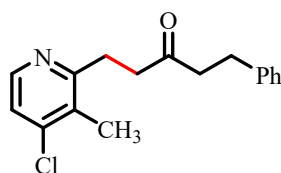
4. A general procedure for Table 1



A solution of substituted 2-methylpyridine N-oxide (0.24 mmol, 1.2 eq.), HNTf₂ (0.22 mmol, 1.1 eq.) in HFIP (0.5 mL) was stirred at room temperature for 15 min. The alkynes (0.20 mmol) and PPh₃AuNTf₂ (5.0 μmol, 2.5 mol%) were added and stirred at room temperature for another 2 hours. Upon completion, the HFIP was removed under reduced pressure. TBAF (0.22 mmol, 1.1 equiv.) and acetone (1 mL) were then added to the residue and stirred at room temperature for 5 min. The crude reaction mixture was then purified by column chromatography to afford the final product.

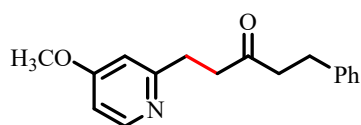


1-phenyl-5-(pyridin-2-yl)pentan-3-one (4a).^[6] Light yellow liquid. (45.5mg, 95%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.48 (dd, *J* = 4.9, 0.8 Hz, 1H), 7.57 (td, *J* = 7.7, 1.8 Hz, 1H), 7.27 (t, *J* = 7.3 Hz, 2H), 7.20 – 7.15 (m, 4H), 7.10 (dd, *J* = 7.5, 4.9 Hz, 1H), 3.07 (t, *J* = 7.2 Hz, 2H), 2.93 – 2.88 (m, 4H), 2.77 (t, *J* = 7.4 Hz, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 209.3, 160.5, 149.3, 141.2, 136.5, 128.6, 128.4, 126.2, 123.3, 121.3, 44.5, 41.8, 31.8, 29.8.

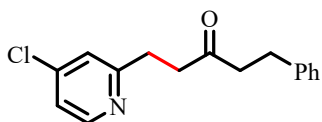


1-(4-chloro-3-methylpyridin-2-yl)-5-phenylpentan-3-one (4b). Yellow liquid. (40.3 mg, 70%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 5.2 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 2H), 7.19 (dd, *J* = 6.6, 4.6 Hz, 3H), 7.12 (d, *J* = 5.3 Hz, 1H), 3.09 (t, *J* = 6.9 Hz, 2H), 2.92 (t, *J* = 5.8 Hz, 4H), 2.86 (dd, *J* = 8.4, 5.7 Hz, 2H), 2.37 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 209.6, 160.0, 146.4, 144.2, 141.3, 130.0,

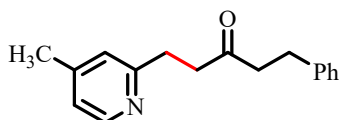
128.6, 128.5, 126.2, 122.4, 44.6, 40.0, 29.9, 29.4, 15.1. **HRMS (ESI-TOF) m/z:** [M + H]⁺ calcd for C₁₇H₁₉ClNO 288.1150; found 288.1145.



1-(4-methoxypyridin-2-yl)-5-phenylpentan-3-one (4c). Colorless liquid. (48.5 mg, 90%, 0.2 mmol scale); **¹H NMR (400 MHz, Chloroform-*d*)** δ 8.29 (d, *J* = 4.3 Hz, 1H), 7.25 (d, *J* = 7.1 Hz, 2H), 7.16 (t, *J* = 8.7 Hz, 3H), 6.70 (s, 1H), 6.65 – 6.64 (m, 1H), 3.82 (s, 3H), 3.00 (t, *J* = 6.3 Hz, 2H), 2.89 (t, *J* = 6.9 Hz, 4H), 2.76 (t, *J* = 7.0 Hz, 2H). **¹³C NMR (101 MHz, Chloroform-*d*)** δ 209.3, 166.1, 162.2, 150.4, 141.2, 128.6, 128.4, 126.2, 109.0, 107.9, 55.1, 44.5, 41.8, 32.0, 29.8. **HRMS (ESI-TOF) m/z:** [M + H]⁺ calcd for C₁₇H₂₀NO₂ 270.1489; found 270.1480.

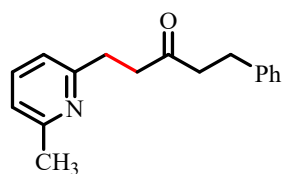


1-(4-chloropyridin-2-yl)-5-phenylpentan-3-one (4d). Colorless liquid. (49.8 mg, 91%, 0.2 mmol scale); **¹H NMR (400 MHz, Chloroform-*d*)** δ 8.35 (d, *J* = 5.3 Hz, 1H), 7.26 (t, *J* = 7.3 Hz, 2H), 7.20 – 7.14 (m, 4H), 7.10 (dd, *J* = 5.3, 1.8 Hz, 1H), 3.03 (t, *J* = 7.0 Hz, 2H), 2.89 (t, *J* = 7.2 Hz, 4H), 2.77 (t, *J* = 7.4 Hz, 2H). **¹³C NMR (101 MHz, Chloroform-*d*)** δ 208.9, 162.2, 150.1, 144.3, 141.1, 128.6, 128.4, 126.2, 123.7, 121.8, 44.4, 41.3, 31.4, 29.8. **HRMS (ESI-TOF) m/z:** [M + Na]⁺ calcd for C₁₆H₁₆ClNONa 296.0813; found 296.0813.

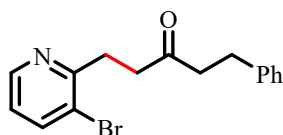


1-(4-methylpyridin-2-yl)-5-phenylpentan-3-one (4e). Colorless liquid. (43.1 mg, 85%, 0.2 mmol scale); **¹H NMR (400 MHz, Chloroform-*d*)** δ 8.33 (d, *J* = 5.0 Hz, 1H), 7.26 (t, *J* = 7.3 Hz, 2H), 7.20 – 7.15 (m, 3H), 6.99 (s, 1H), 6.92 (d, *J* = 5.0 Hz, 1H), 3.01 (t, *J* = 7.3 Hz, 2H), 2.92 – 2.87 (m, 4H), 2.78 – 2.75 (m, 2H), 2.30 (s, 3H). **¹³C NMR (101 MHz, Chloroform-*d*)** δ 209.4, 160.3, 149.0, 147.6, 141.2, 128.6, 128.4,

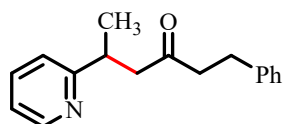
126.2, 124.2, 122.4, 44.5, 41.9, 31.7, 29.8, 21.1. **HRMS (ESI-TOF) m/z:** [M + Na]⁺ calcd for C₁₇H₁₉NONa 276.1359; found 276.1358.



1-(6-methylpyridin-2-yl)-5-phenylpentan-3-one (4f) [7]. Colorless liquid. (48.6 mg, 96%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.45 (t, *J* = 7.7 Hz, 1H), 7.28 – 7.25 (m, 2H), 7.20 – 7.15 (m, 3H), 6.95 (d, *J* = 7.6 Hz, 2H), 3.03 (t, *J* = 7.3 Hz, 2H), 2.88 (dt, *J* = 14.1, 7.4 Hz, 4H), 2.80 – 2.76 (m, 2H), 2.49 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 209.4, 159.9, 157.9, 141.3, 136.7, 128.6, 128.4, 126.2, 120.8, 120.1, 44.6, 42.2, 32.0, 29.8, 24.6.

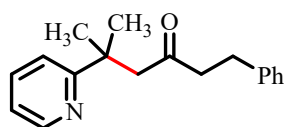


1-(3-bromopyridin-2-yl)-5-phenylpentan-3-one (4g). Yellow liquid. (42.0 mg, 66%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.36 – 8.30 (m, 1H), 7.75 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.16 (d, *J* = 7.3 Hz, 3H), 6.95 (dd, *J* = 8.0, 4.7 Hz, 1H), 3.19 (t, *J* = 7.1 Hz, 2H), 2.89 (dd, *J* = 12.8, 6.9 Hz, 4H), 2.86 – 2.82 (m, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 209.1, 158.5, 147.5, 141.4, 140.1, 128.6, 128.5, 126.2, 122.7, 121.7, 44.6, 39.9, 31.2, 29.9. **HRMS (ESI-TOF) m/z:** [M + H]⁺ calcd for C₁₆H₁₇BrNO 318.0488; found 318.0479.

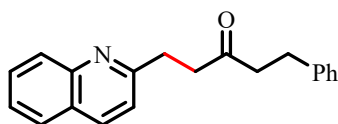


1-phenyl-5-(pyridin-2-yl)hexan-3-one (4h). Colorless liquid. (38.0 mg, 75%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.50 (s, 1H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.14 (dt, *J* = 18.6, 9.4 Hz, 5H), 3.47 (q, *J* = 6.3 Hz, 1H), 3.09 (dd, *J* = 16.8, 7.1 Hz, 1H), 2.84 (t, *J* = 6.8 Hz, 2H), 2.73 – 2.63 (m, 3H), 1.27 (d, *J* = 6.0 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 209.3, 164.9, 149.2, 141.2,

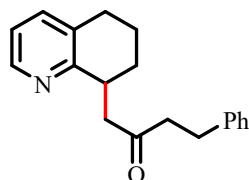
136.6, 128.6, 128.4, 126.1, 122.5, 121.5, 49.1, 44.9, 37.1, 29.7, 21.2. **HRMS (ESI-TOF) m/z:** $[M + Na]^+$ calcd for $C_{17}H_{19}NONa$ 276.1359; found 276.1352.



5-methyl-1-phenyl-5-(pyridin-2-yl)hexan-3-one (4i). Colorless liquid. (16.0 mg, 30%, 0.2 mmol scale); 1H NMR (400 MHz, Chloroform-*d*) δ 8.50 (s, 1H), 7.31 – 7.28 (m, 4H), 7.21 (d, $J = 6.8$ Hz, 1H), 7.16 (d, $J = 7.1$ Hz, 2H), 7.06 – 7.05 (m, 1H), 3.71 (s, 2H), 2.94 (d, $J = 7.3$ Hz, 2H), 2.80 (t, $J = 7.0$ Hz, 2H), 1.20 (d, $J = 5.5$ Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 206.7, 165.4, 148.4, 140.8, 138.5, 128.7, 128.5, 126.8, 126.4, 121.2, 47.2, 43.9, 31.6, 30.0, 22.2. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ calcd for $C_{18}H_{22}NO$ 268.1696; found 268.1687.

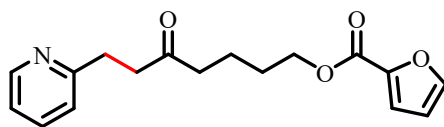


1-phenyl-5-(quinolin-2-yl)pentan-3-one (4j) ¹⁸¹. Colorless liquid. (42.8 mg, 74%, 0.2 mmol scale); 1H NMR (400 MHz, Chloroform-*d*) δ 8.04 (d, $J = 8.4$ Hz, 1H), 7.97 (d, $J = 8.5$ Hz, 1H), 7.77 (d, $J = 8.1$ Hz, 1H), 7.67 (t, $J = 7.7$ Hz, 1H), 7.48 (t, $J = 7.5$ Hz, 1H), 7.31 – 7.24 (m, 3H), 7.18 (d, $J = 7.5$ Hz, 3H), 3.28 (t, $J = 7.1$ Hz, 2H), 3.03 (t, $J = 7.0$ Hz, 2H), 2.95 – 2.91 (m, 2H), 2.88 – 2.84 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 209.4, 161.0, 147.9, 141.3, 136.3, 129.5, 128.9, 128.6, 128.4, 127.7, 126.9, 126.2, 125.9, 121.9, 44.6, 41.3, 32.5, 29.9.

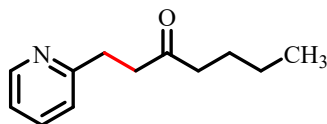


4-phenyl-1-(5,6,7,8-tetrahydroquinolin-8-yl)butan-2-one (4k). Colorless liquid. (53.1mg,95%, 0.2 mmol scale); 1H NMR (400 MHz, Chloroform-*d*) δ 8.33 – 8.28 (m, 1H), 7.30 (dd, $J = 23.8, 7.6$ Hz, 3H), 7.19 (dd, $J = 12.4, 7.1$ Hz, 3H), 7.01 (dd, $J = 7.6, 4.7$ Hz, 1H), 3.50 – 3.39 (m, 1H), 3.18 (dd, $J = 16.5, 5.0$ Hz, 1H), 2.99 – 2.92 (m, 2H), 2.92 – 2.84 (m, 1H), 2.83 – 2.70 (m, 3H), 2.58 (dd, $J = 16.5, 8.2$ Hz, 1H), 2.11 – 1.98

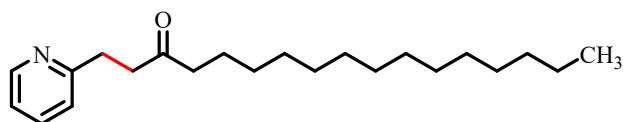
(m, 1H), 1.89 – 1.80 (m, 1H), 1.80 – 1.68 (m, 1H), 1.62 – 1.48 (m, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 209.6, 159.0, 146.8, 141.5, 136.8, 132.4, 128.6, 128.5, 126.1, 121.2, 48.3, 44.9, 37.5, 30.0, 29.2, 21.1. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₉H₂₁NONa 302.1515; found 302.1515.



5-oxo-7-(pyridin-2-yl)heptyl furan-2-carboxylate (4l). Colorless liquid. (49.4 mg, 82%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.48 – 8.46 (m, 1H), 7.58 – 7.54 (m, 2H), 7.17 – 7.15 (m, 2H), 7.08 (dd, *J* = 7.2, 4.7 Hz, 1H), 6.48 (dd, *J* = 3.5, 1.7 Hz, 1H), 4.27 (t, *J* = 6.1 Hz, 2H), 3.05 (t, *J* = 7.2 Hz, 2H), 2.91 (t, *J* = 7.2 Hz, 2H), 2.50 (t, *J* = 6.8 Hz, 2H), 1.70 (dt, *J* = 6.3, 2.8 Hz, 4H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 160.5, 158.9, 149.2, 146.4, 144.8, 136.5, 123.4, 121.4, 118.0, 111.9, 64.7, 42.3, 41.6, 31.8, 28.2, 20.2. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₇H₁₉NO₄Na 324.1206; found 324.1197.

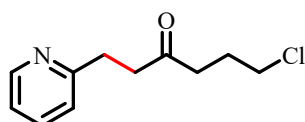


1-(pyridin-2-yl)heptan-3-one (4m) ¹⁹. Colorless liquid. (33.3 mg, 87%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.49 (dd, *J* = 4.9, 0.8 Hz, 1H), 7.56 (td, *J* = 7.7, 1.8 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 1H), 7.09 (dd, *J* = 7.5, 4.9 Hz, 1H), 3.05 (t, *J* = 7.3 Hz, 2H), 2.91 (t, *J* = 7.2 Hz, 2H), 2.42 (t, *J* = 7.5 Hz, 2H), 1.54 (dt, *J* = 15.1, 7.5 Hz, 2H), 1.28 (dq, *J* = 14.6, 7.3 Hz, 2H), 0.87 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 210.6, 160.7, 149.3, 136.5, 123.4, 121.3, 42.8, 41.7, 31.9, 26.1, 22.4, 14.0.

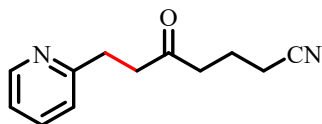


1-(pyridin-2-yl)heptadecan-3-one (4n). Colorless solid. (56.4 mg, 85%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.48 (d, *J* = 3.7 Hz, 1H), 7.56 (td, *J* = 7.7, 1.8 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 1H), 7.08 (dd, *J* = 7.0, 5.3 Hz, 1H), 3.04 (t, *J* =

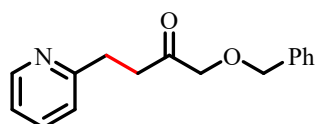
7.3 Hz, 2H), 2.90 (t, $J = 7.2$ Hz, 2H), 2.40 (t, $J = 7.5$ Hz, 2H), 1.56 – 1.52 (m, 2H), 1.23 (s, 22H), 0.86 (t, $J = 6.9$ Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 210.6, 160.7, 149.2, 136.5, 123.4, 121.3, 43.1, 41.7, 31.9 (d, $J = 20.7$ Hz), 30.2 – 29.1 (m), 24.0, 22.8, 14.2. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{38}\text{NO}_4$ 332.2948; found 332.2940.



6-chloro-1-(pyridin-2-yl)hexan-3-one (4o). Colorless liquid. (39.4 mg, 93%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.49 (d, $J = 4.8$ Hz, 1H), 7.57 (td, $J = 7.7, 1.8$ Hz, 1H), 7.17 (d, $J = 7.8$ Hz, 1H), 7.09 (dd, $J = 7.0, 5.4$ Hz, 1H), 3.55 (t, $J = 6.3$ Hz, 2H), 3.07 (t, $J = 7.2$ Hz, 2H), 2.93 (t, $J = 7.1$ Hz, 2H), 2.65 (t, $J = 7.0$ Hz, 2H), 2.04 (p, $J = 6.7$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 209.1, 160.3, 149.2, 136.5, 123.3, 121.4, 44.6, 41.6, 39.5, 31.7, 26.4. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{11}\text{H}_{15}\text{ClNO}$ 212.0837; found 212.0832.

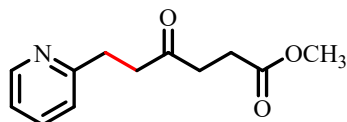


5-oxo-7-(pyridin-2-yl) heptanenitrile (4p). Colorless liquid. (34.6 mg, 90%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.48 (d, $J = 4.7$ Hz, 1H), 7.57 (td, $J = 7.6, 1.8$ Hz, 1H), 7.17 (d, $J = 7.8$ Hz, 1H), 7.10 (dd, $J = 7.3, 5.1$ Hz, 1H), 3.09 (t, $J = 7.0$ Hz, 2H), 2.90 (t, $J = 7.0$ Hz, 2H), 2.67 (t, $J = 6.8$ Hz, 2H), 2.40 (t, $J = 7.0$ Hz, 2H), 1.92 (p, $J = 6.9$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.5, 160.1, 149.2, 136.5, 123.3, 121.5, 119.5, 41.3, 40.6, 31.7, 19.5, 16.5. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{15}\text{N}_2\text{O}$ 203.1179; found 203.1170.

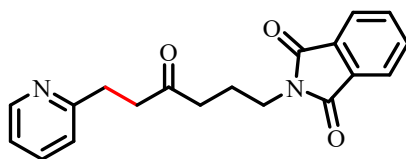


1-(benzyloxy)-4-(pyridin-2-yl)butan-2-one (4q) ^{16l}. Colorless liquid. (47.0 mg, 92%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.47 (d, $J = 4.5$ Hz, 1H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.35 – 7.28 (m, 5H), 7.17 (d, $J = 7.8$ Hz, 1H), 7.10 – 7.07 (m, 1H),

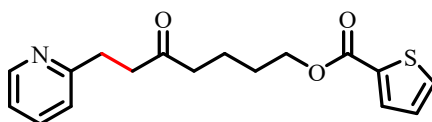
4.58 (s, 2H), 4.12 (s, 2H), 3.11 (t, $J = 7.1$ Hz, 2H), 2.95 (t, $J = 7.1$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.1, 160.2, 149.3, 137.4, 136.5, 128.6, 128.1 (d, $J = 3.3$ Hz), 123.3, 121.4, 75.2, 73.4, 37.8, 31.3.



1-(pyridin-2-yl)heptan-3-one (4r). Colorless liquid. (39.8 mg, 90%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.5 (dd, $J = 4.9, 1.6$ Hz, 1H), 7.6 (td, $J = 7.7, 1.8$ Hz, 1H), 7.2 (d, $J = 7.8$ Hz, 1H), 7.1 (dd, $J = 7.5, 4.9$ Hz, 1H), 3.65 (s, 3H), 3.07 (t, $J = 6.9$ Hz, 2H), 2.96 (t, $J = 6.9$ Hz, 2H), 2.77 (t, $J = 6.6$ Hz, 2H), 2.58 (t, $J = 6.5$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.2, 173.4, 160.4, 149.3, 136.5, 123.3, 121.4, 51.9, 41.5, 37.3, 31.7, 27.9. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_3\text{Na}$ 244.0944; found 244.0942.

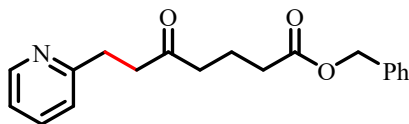


2-(4-oxo-6-(pyridin-2-yl)hexyl)isoindoline-1,3-dione (4s). White solid. (61.9 mg, 96%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.46 (d, $J = 4.3$ Hz, 1H), 7.83 – 7.82 (m, 2H), 7.71 – 7.69 (m, 2H), 7.55 (t, $J = 7.6$ Hz, 1H), 7.15 (d, $J = 7.7$ Hz, 1H), 7.07 (t, $J = 5.9$ Hz, 1H), 3.69 (t, $J = 6.6$ Hz, 2H), 3.04 (t, $J = 7.1$ Hz, 2H), 2.90 (t, $J = 7.1$ Hz, 2H), 2.50 (t, $J = 7.1$ Hz, 2H), 1.95 (p, $J = 6.5$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.8, 168.6, 160.5, 149.3, 136.4, 134.1, 132.2, 123.4, 123.3, 121.3, 41.6, 39.9, 37.3, 31.7, 22.8. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_3\text{Na}$ 345.1210; found 345.1204.

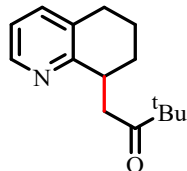


5-oxo-7-(pyridin-2-yl)heptyl thiophene-2-carboxylate (4t). Colorless liquid. (46.3mg, 73%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.47 (d, $J = 4.8$ Hz, 1H), 7.77 (dd, $J = 3.7, 1.3$ Hz, 1H), 7.57 – 7.52 (m, 2H), 7.16 (d, $J = 7.8$ Hz, 1H), 7.07 (td, $J = 5.3, 1.6$ Hz, 2H), 4.27 – 4.24 (m, 2H), 3.06 (t, $J = 7.2$ Hz, 2H), 2.91

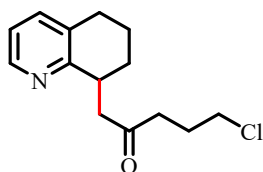
(t, $J = 7.2$ Hz, 2H), 2.51 (t, $J = 6.9$ Hz, 2H), 1.72 – 1.70 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 209.8, 162.4, 160.5, 149.3, 136.5, 134.0, 133.5, 132.4, 127.9, 123.4, 121.4, 64.9, 42.3, 41.6, 31.8, 28.3, 20.3. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_3\text{SNa}$ 340.0978; found 340.0977.



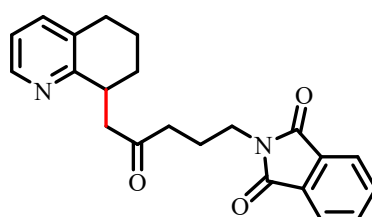
benzyl 5-oxo-7-(pyridin-2-yl)heptanoate (4u). Colorless liquid. (59.2 mg, 95%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.47 – 8.46 (m, 1H), 7.56 (td, $J = 7.7, 1.8$ Hz, 1H), 7.35 – 7.30 (m, 5H), 7.16 (d, $J = 7.8$ Hz, 1H), 7.08 (dd, $J = 7.5, 4.9$ Hz, 1H), 5.10 (s, 2H), 3.05 (t, $J = 7.2$ Hz, 2H), 2.88 (t, $J = 7.2$ Hz, 2H), 2.50 (t, $J = 7.2$ Hz, 2H), 2.36 (t, $J = 7.3$ Hz, 2H), 1.91 (p, $J = 7.3$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 209.4, 173.1, 160.5, 149.3, 136.4, 136.1, 128.7, 128.3, 123.3, 121.3, 66.3, 41.6 (d, $J = 13.9$ Hz), 33.4, 31.7, 19.0. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{21}\text{NO}_3\text{Na}$ 334.1414; found 334.1413.



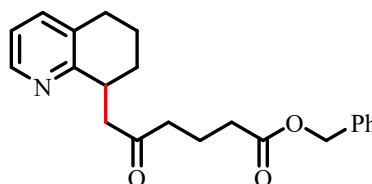
3,3-dimethyl-1-(5,6,7,8-tetrahydroquinolin-8-yl)butan-2-one (4v). Colorless liquid. (36.6 mg, 79%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.34 – 8.32 (m, 1H), 7.33 (d, $J = 7.6$ Hz, 1H), 7.00 (dd, $J = 7.6, 4.7$ Hz, 1H), 3.48 – 3.46 (m, 1H), 3.25 (dd, $J = 17.7, 3.6$ Hz, 1H), 2.85 – 2.74 (m, 3H), 2.05 – 2.00 (m, 1H), 1.87 – 1.73 (m, 2H), 1.55 – 1.47 (m, 1H), 1.16 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 215.1, 159.6, 146.9, 136.7, 132.6, 121.1, 44.3, 42.2, 36.8, 29.4, 28.9, 26.6, 21.0. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{22}\text{NO}$ 232.1696; found 232.1694.



5-chloro-1-(5,6,7,8-tetrahydroquinolin-8-yl)pentan-2-one (4w). Colorless liquid. (47.8 mg, 95%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 4.2 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.00 (dd, *J* = 7.6, 4.7 Hz, 1H), 3.60 (t, *J* = 6.3 Hz, 2H), 3.44 (dt, *J* = 13.9, 6.1 Hz, 1H), 3.13 (dd, *J* = 16.3, 5.6 Hz, 1H), 2.82 – 2.74 (m, 3H), 2.66 – 2.55 (m, 2H), 2.13 – 2.02 (m, 3H), 1.90 – 1.83 (m, 1H), 1.80 – 1.72 (m, 1H), 1.61 – 1.52 (m, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 209.3, 158.9, 146.7, 136.8, 132.4, 121.3, 48.1, 44.7, 39.9, 37.7, 29.3, 29.1, 26.6, 21.2. HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₄H₁₉ClNO 252.1150; found 252.1149.

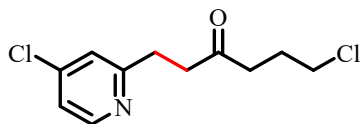


2-(4-oxo-5-(5,6,7,8-tetrahydroquinolin-8-yl)pentyl)isoindoline-1,3-dione (4x). White solid. (66.7 mg, 92%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.30 – 8.29 (m, 1H), 7.84 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.71 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 1H), 6.98 (dd, *J* = 7.6, 4.7 Hz, 1H), 3.73 (td, *J* = 6.8, 1.8 Hz, 2H), 3.41 (ddd, *J* = 13.6, 8.4, 5.4 Hz, 1H), 3.16 (dd, *J* = 16.6, 5.0 Hz, 1H), 2.77 – 2.74 (m, 2H), 2.64 – 2.50 (m, 3H), 2.08 – 1.97 (m, 3H), 1.85 – 1.80 (m, 1H), 1.80 – 1.70 (m, 1H), 1.59 – 1.55 (m, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 209.1, 168.5, 159.0, 146.7, 136.7, 134.0, 132.3, 132.2, 123.3, 121.1, 47.9, 40.3, 37.5, 37.4, 29.1, 22.9, 21.0. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₂₂H₂₂N₂O₃Na 385.1523; found 385.1516.

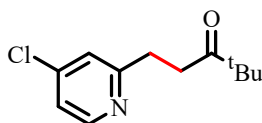


benzyl 5-oxo-6-(5,6,7,8-tetrahydroquinolin-8-yl)hexanoate (4y). Colorless liquid. (58.3 mg, 83%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.29 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.35 – 7.31 (m, 6H), 6.99 (dd, *J* = 7.6, 4.7 Hz, 1H), 5.11 (s, 2H), 3.50 – 3.43 (m, 1H), 3.12 (dd, *J* = 16.4, 5.3 Hz, 1H), 2.75 (t, *J* = 7.1 Hz, 2H), 2.64 – 2.49 (m, 3H), 2.45 – 2.41 (m, 2H), 2.05 – 2.00 (m, 1H), 1.94 (p, *J* = 7.3 Hz, 2H), 1.85 – 1.84

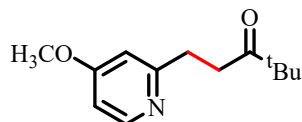
(m, 1H), 1.83 – 1.75 (m, 1H), 1.58 – 1.54 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 209.6, 173.3, 159.0, 146.7, 136.7, 136.1, 132.4, 128.7, 128.32, 128.30, 121.2, 66.3, 48.1, 42.0, 37.5, 33.4, 29.3, 29.1, 21.1, 19.1. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{25}\text{NO}_3\text{Na}$ 374.1727; found 374.1725.



6-chloro-1-(4-chloropyridin-2-yl)hexan-3-one (4z). Colorless liquid. (40.4 mg, 82%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.36 (d, $J = 5.4$ Hz, 1H), 7.20 (d, $J = 1.9$ Hz, 1H), 7.11 (dd, $J = 5.4, 1.9$ Hz, 1H), 3.55 (t, $J = 6.3$ Hz, 2H), 3.05 (t, $J = 7.0$ Hz, 2H), 2.92 (t, $J = 7.0$ Hz, 2H), 2.65 (t, $J = 7.0$ Hz, 2H), 2.03 (p, $J = 6.7$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.7, 162.1, 150.1, 144.3, 123.6, 121.8, 44.5, 41.1, 39.5, 31.5, 26.4. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{14}\text{Cl}_2\text{NO}$ 246.0447; found 246.0439.

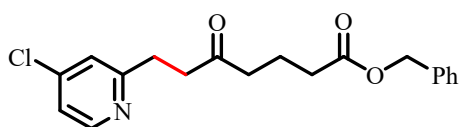


1-(4-chloropyridin-2-yl)-4,4-dimethylpentan-3-one (4aa). White solid. (40.2 mg, 89%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.37 (d, $J = 5.4$ Hz, 1H), 7.21 (d, $J = 1.9$ Hz, 1H), 7.10 (dd, $J = 5.4, 2.0$ Hz, 1H), 3.00 – 2.99 (m, 4H), 1.12 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 214.9, 162.8, 150.1, 144.3, 123.8, 121.7, 44.2, 35.7, 31.9, 26.6. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{17}\text{ClNO}$ 226.0993; found 226.0993.

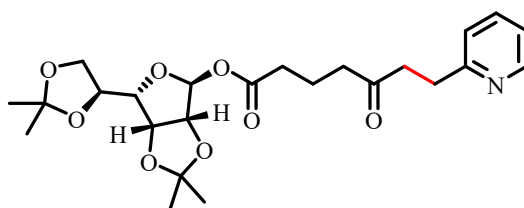


1-(4-methoxypyridin-2-yl)-4,4-dimethylpentan-3-one (4ab). Colorless liquid. (35.4 mg, 80%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.30 (d, $J = 5.8$ Hz, 1H), 6.70 (d, $J = 2.5$ Hz, 1H), 6.63 (dd, $J = 5.8, 2.5$ Hz, 1H), 3.82 (s, 3H), 2.97 (s, 4H), 1.11 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 215.3, 166.1, 162.8, 150.5, 109.1,

107.8, 55.1, 44.2, 36.2, 32.4, 26.5. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ calcd for $C_{13}H_{20}NO_2$ 222.1489; found 222.1489.

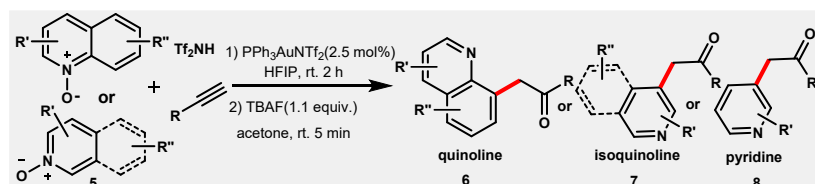


benzyl 7-(4-chloropyridin-2-yl)-5-oxoheptanoate (4ac). Colorless liquid. (60.2 mg, 87%, 0.2 mmol scale); 1H NMR (400 MHz, Chloroform-*d*) δ 8.34 (d, $J = 5.4$ Hz, 1H), 7.35 – 7.32 (m, 5H), 7.19 (d, $J = 1.7$ Hz, 1H), 7.09 (dd, $J = 5.4, 1.9$ Hz, 1H), 5.10 (s, 2H), 3.02 (t, $J = 7.0$ Hz, 2H), 2.87 (t, $J = 7.1$ Hz, 2H), 2.50 (t, $J = 7.2$ Hz, 2H), 2.37 (t, $J = 7.3$ Hz, 2H), 1.91 (p, $J = 7.3$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.9, 173.1, 162.2, 150.1, 144.3, 136.0, 128.7, 128.3, 123.6, 121.8, 66.3, 41.6, 41.0, 33.3, 31.4, 19.0. **HRMS (ESI-TOF) m/z:** $[M + Na]^+$ calcd for $C_{19}H_{20}ClNO_3Na$ 368.1024; found 368.1020.

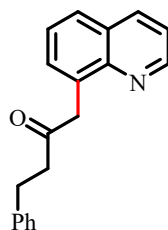


(3aR,4S,6S,6aR)-6-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl 5-oxo-7-(pyridin-2-yl)heptanoate (15). Light yellow liquid. (75.1 mg, 81%, 0.2 mmol scale); 1H NMR (400 MHz, Chloroform-*d*) δ 8.46 (d, $J = 4.0$ Hz, 1H), 7.58 (td, $J = 7.7, 1.8$ Hz, 1H), 7.18 (d, $J = 7.8$ Hz, 1H), 7.11 (dd, $J = 8.0, 4.4$ Hz, 1H), 6.15 (q, $J = 3.8$ Hz, 1H), 4.93 – 4.90 (m, 1H), 4.68 (dd, $J = 5.9, 3.7$ Hz, 1H), 4.13 – 4.10 (m, 1H), 4.11 – 4.00 (m, 1H), 3.86 – 3.83 (m, 1H), 3.78 – 3.74 (m, 1H), 3.06 – 3.02 (m, 3H), 2.90 – 2.87 (m, 3H), 2.53 – 2.51 (m, 2H), 2.33 – 2.29 (m, 2H), 1.90 – 1.87 (m, 2H), 1.47 (d, $J = 3.7$ Hz, 3H), 1.33 (d, $J = 3.7$ Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 209.6, 171.8, 160.3, 149.1, 136.9, 123.6, 121.6, 113.3, 100.5, 84.8, 81.0, 79.9, 69.8, 63.5, 41.8, 41.3, 33.4, 31.7, 26.1, 24.9, 18.9. **HRMS (ESI-TOF) m/z:** $[M + Na]^+$ calcd for $C_{24}H_{33}NO_8Na$ 486.2098; found 486.2096.

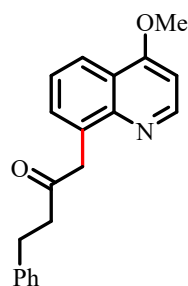
5. A general procedure for Table 2



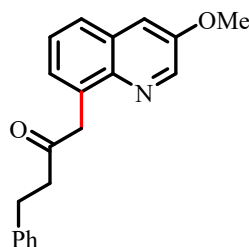
A solution of substituted quinoline N-oxide (0.24 mmol, 1.2 eq.), HNTf₂ (0.22 mmol, 1.1 eq.) in HFIP (0.5 mL) was stirred at room temperature for 15 min. The alkynes (0.20 mmol) and PPh₃AuNTf₂ (5.0 μmol, 2.5 mol%) were added and stirred at room temperature for another 2 hours. Upon completion, the HFIP was removed under reduced pressure. TBAF (1.1 eq.) and acetone (1 mL) were then added to the residue and stirred at room temperature for 5 min. The crude reaction mixture was then purified by column chromatography to afford the final product.



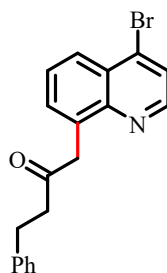
4-phenyl-1-(quinolin-8-yl)butan-2-one (6a). White solid. (46.3 mg, 84%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.86 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.75 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.55 (d, *J* = 5.5 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.26 – 7.22 (m, 2H), 7.18 – 7.14 (m, 3H), 4.32 (s, 2H), 2.92 (s, 4H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 208.4, 149.8, 146.8, 141.5, 136.4, 134.2, 130.8, 128.6, 128.53, 128.51, 127.4, 126.5, 126.1, 121.3, 45.8, 44.2, 30.0. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₉H₁₇NONa 298.1202; found 298.1204.



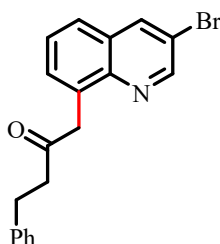
1-(4-methoxyquinolin-8-yl)-4-phenylbutan-2-one (6b). White solid. (50.7 mg, 83%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.70 (d, $J = 5.2$ Hz, 1H), 8.14 (dd, $J = 8.3, 1.3$ Hz, 1H), 7.52 (d, $J = 7.0$ Hz, 1H), 7.47 – 7.40 (m, 1H), 7.23 (d, $J = 7.5$ Hz, 2H), 7.15 (dd, $J = 12.6, 7.0$ Hz, 3H), 6.74 (d, $J = 5.2$ Hz, 1H), 4.29 (s, 2H), 4.03 (s, 3H), 2.91 – 2.89 (m, 4H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 208.5, 162.6, 147.7, 141.5, 133.6, 131.1, 128.52, 128.48, 126.0, 125.4, 121.7, 121.4, 100.3, 55.9, 46.2, 44.0, 29.9. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_2\text{Na}$ 328.1308; found 328.1299.



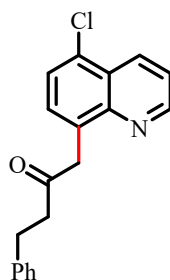
1-(3-methoxyquinolin-8-yl)-4-phenylbutan-2-one (6c). White solid. (28.0mg, 46%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.61 (d, $J = 2.9$ Hz, 1H), 7.65 (dd, $J = 8.1, 1.4$ Hz, 1H), 7.46 – 7.43 (m, 1H), 7.39 – 7.36 (m, 2H), 7.26 – 7.23 (m, 2H), 7.18 – 7.13 (m, 3H), 4.29 (s, 2H), 3.94 (s, 3H), 2.94 – 2.86 (m, 4H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 208.4, 153.3, 143.8, 141.5, 134.0, 129.2, 128.51, 128.48, 128.1, 127.1, 126.8, 126.4, 126.0, 112.6, 55.6, 46.0, 44.0, 29.9. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_2\text{Na}$ 328.1308; found 328.1309.



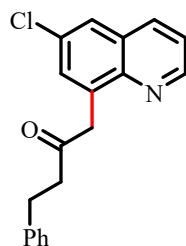
1-(4-bromoquinolin-8-yl)-4-phenylbutan-2-one (6e). White solid. (25.5mg, 36%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.58 (d, $J = 4.6$ Hz, 1H), 8.13 (dd, $J = 6.3, 3.6$ Hz, 1H), 7.68 (d, $J = 4.6$ Hz, 1H), 7.58 (t, $J = 6.3$ Hz, 2H), 7.26 (t, $J = 7.2$ Hz, 2H), 7.24 – 7.15 (m, 3H), 4.30 (s, 2H), 2.93 (s, 4H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 207.9, 149.1, 147.5, 141.4, 134.8, 134.5, 131.8, 128.5, 128.2, 127.7, 126.5, 126.1, 125.3, 46.0, 44.2, 29.9. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{16}\text{BrNONa}$ 376.0307; found 376.0304.



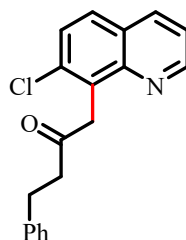
1-(3-bromoquinolin-8-yl)-4-phenylbutan-2-one (6f). White solid. (29.7 mg, 42%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.80 (d, $J = 2.3$ Hz, 1H), 8.27 (d, $J = 2.3$ Hz, 1H), 7.65 (dd, $J = 7.9, 1.7$ Hz, 1H), 7.55 – 7.48 (m, 2H), 7.28 – 7.24 (m, 2H), 7.20 – 7.15 (m, 3H), 4.27 (s, 2H), 2.93 (s, 4H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 207.8, 150.7, 144.8, 141.3, 137.5, 134.5, 131.1, 129.4, 128.5, 127.7, 126.5, 126.1, 117.6, 45.7, 44.2, 29.9. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{16}\text{BrNONa}$ 376.0307; found 376.0302.



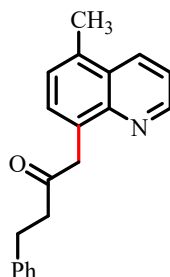
1-(5-chloroquinolin-8-yl)-4-phenylbutan-2-one (6g). White solid. (24.2 mg, 39%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.88 (dd, $J = 4.1, 1.3$ Hz, 1H), 8.57 (dd, $J = 8.5, 1.4$ Hz, 1H), 7.57 (d, $J = 7.7$ Hz, 1H), 7.50 (dd, $J = 8.5, 4.2$ Hz, 1H), 7.45 (d, $J = 7.7$ Hz, 1H), 7.26 (t, $J = 7.2$ Hz, 2H), 7.20 – 7.15 (m, 3H), 4.28 (s, 2H), 2.94 (s, 4H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 207.8, 150.3, 147.3, 141.3, 133.6, 133.2, 130.6, 130.4, 128.5, 126.6, 126.5, 126.1, 122.0, 45.6, 44.3, 29.9. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{16}\text{ClNONa}$ 332.0813; found 332.0806.



1-(6-chloroquinolin-8-yl)-4-phenylbutan-2-one (6h). White solid. (21.1 mg, 34%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.82 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.05 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.73 (d, $J = 2.3$ Hz, 1H), 7.50 (d, $J = 2.3$ Hz, 1H), 7.41 (dd, $J = 8.3, 4.2$ Hz, 1H), 7.26 (t, $J = 7.2$ Hz, 2H), 7.20 – 7.16 (m, 3H), 4.27 (s, 2H), 2.95 (s, 4H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 207.4, 149.9, 145.2, 141.3, 136.4, 135.5, 132.0, 131.5, 129.1, 128.5 (d, $J = 2.9$ Hz), 126.2, 125.9, 122.2, 45.4, 44.4, 29.9. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{16}\text{ClN}\text{ONa}$ 332.0813; found 332.0812.

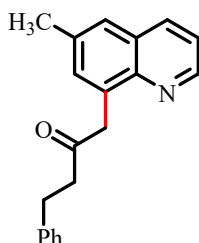


1-(7-chloroquinolin-8-yl)-4-phenylbutan-2-one (6i). White solid. (44.6 mg, 72%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.87 (dd, $J = 4.2, 1.8$ Hz, 1H), 8.12 (dd, $J = 8.3, 1.8$ Hz, 1H), 7.69 (d, $J = 8.8$ Hz, 1H), 7.55 (d, $J = 8.8$ Hz, 1H), 7.39 (dd, $J = 8.2, 4.2$ Hz, 1H), 7.29 – 7.25 (m, 2H), 7.19 (d, $J = 6.8$ Hz, 3H), 4.60 (s, 2H), 2.99 – 2.90 (m, 4H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 206.6, 150.6, 147.5, 141.4, 135.8, 132.4, 128.54, 128.52, 128.0, 127.9, 127.0, 126.1, 121.3, 44.3, 42.8, 29.9. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{16}\text{ClN}\text{ONa}$ 332.0813; found 332.0813.

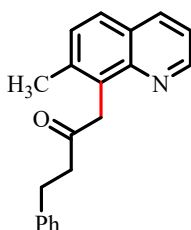


1-(5-methylquinolin-8-yl)-4-phenylbutan-2-one (6j). White solid. (38.2 mg, 66%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.86 (dd, $J = 4.1, 1.7$ Hz, 1H),

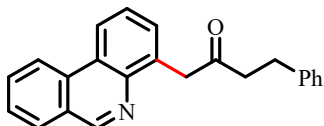
8.31 (dd, $J = 8.5, 1.7$ Hz, 1H), 7.44 – 7.40 (m, 2H), 7.31 (d, $J = 7.7$ Hz, 1H), 7.26 – 7.22 (m, 2H), 7.18 – 7.13 (m, 3H), 4.28 (s, 2H), 2.95 – 2.87 (m, 4H), 2.67 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.7, 149.2, 146.9, 141.5, 134.1, 132.8, 132.3, 130.4, 128.53, 128.48, 127.9, 126.9, 126.0, 120.8, 45.9, 44.0, 30.0, 18.7. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{NONa}$ 312.1359; found 312.1354.



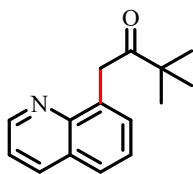
1-(6-methylquinolin-8-yl)-4-phenylbutan-2-one (6k). White solid. (23.2 mg, 40%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.79 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.05 (dd, $J = 8.2, 1.5$ Hz, 1H), 7.50 (s, 1H), 7.38 – 7.34 (m, 2H), 7.26 – 7.23 (m, 2H), 7.18 – 7.14 (m, 3H), 4.29 (s, 2H), 2.92 (s, 4H), 2.50 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.5, 148.9, 141.5, 136.3, 135.8, 133.7, 133.1, 128.7, 128.53, 128.49, 126.3, 126.0, 121.3, 45.7, 44.1, 29.9, 21.7. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{20}\text{NO}$ 290.1539; found 290.1536.



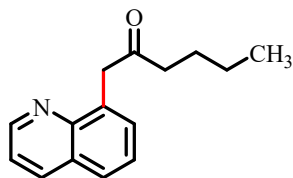
1-(7-methylquinolin-8-yl)-4-phenylbutan-2-one (6l). White solid. (46.3mg, 80%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.84 (dd, $J = 4.2, 1.8$ Hz, 1H), 8.09 (dd, $J = 8.2, 1.8$ Hz, 1H), 7.65 (d, $J = 8.4$ Hz, 1H), 7.39 (d, $J = 8.4$ Hz, 1H), 7.33 (dd, $J = 8.2, 4.2$ Hz, 1H), 7.23 (d, $J = 7.5$ Hz, 2H), 7.18 – 7.12 (m, 3H), 4.48 (s, 2H), 2.94 – 2.84 (m, 4H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.4, 149.7, 147.0, 141.5, 138.5, 136.2, 131.7, 129.8, 128.5, 126.8, 126.6, 126.0, 120.4, 43.8, 42.3, 30.0, 20.6. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{20}\text{NO}$ 290.1539; found 290.1536.



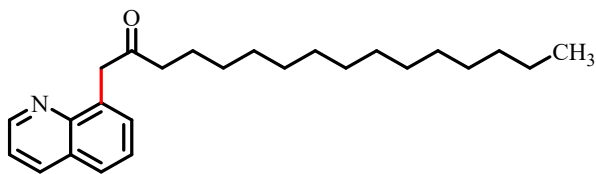
1-(phenanthridin-4-yl)-4-phenylbutan-2-one (6m) ¹⁰¹. Light yellow liquid. (52.7 mg, 81%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 9.22 (s, 1H), 8.62 (d, *J* = 8.3 Hz, 1H), 8.57 – 8.49 (m, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.87 (t, *J* = 7.3 Hz, 1H), 7.72 (t, *J* = 7.4 Hz, 1H), 7.67 – 7.56 (m, 2H), 7.29 – 7.20 (m, 2H), 7.16 (t, *J* = 6.5 Hz, 3H), 4.39 (s, 2H), 2.94 (s, 4H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 208.5, 152.8, 141.5, 134.9, 132.8, 131.1, 130.3, 128.9, 128.6, 128.5, 127.7, 126.9, 126.4, 126.0, 124.4, 122.2, 121.8, 46.5, 44.1, 30.0.



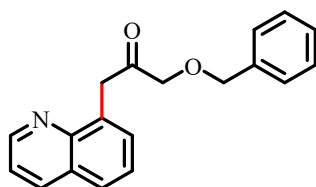
3,3-dimethyl-1-(quinolin-8-yl)butan-2-one (6n) ¹⁰¹. Colorless liquid. (38.2 mg, 84%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.84 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.73 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.36 (dd, *J* = 8.2, 4.2 Hz, 1H), 4.49 (s, 2H), 1.33 (s, 9H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 214.0, 149.5, 146.8, 136.3, 135.0, 130.7, 128.4, 127.0, 126.3, 121.1, 44.9, 39.3, 26.9.



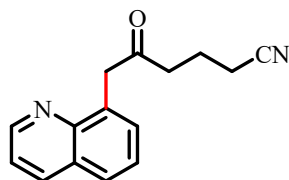
1-(quinolin-8-yl)hexan-2-one (6o) ¹⁰¹. Colorless liquid. (36.8mg, 81%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.88 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.75 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.58 (d, *J* = 5.8 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 4.33 (s, 2H), 2.58 (t, *J* = 7.4 Hz, 2H), 1.59 – 1.55 (m, 2H), 1.34 – 1.24 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 209.6, 149.8, 146.8, 136.4, 134.5, 130.7, 128.6, 127.3, 126.4, 121.3, 45.6, 42.5, 26.1, 22.4, 14.0.



1-(quinolin-8-yl)hexadecan-2-one (6p). Colorless solid. (51.5mg, 70%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.88 (dd, $J = 4.2, 1.8$ Hz, 1H), 8.14 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.75 (dd, $J = 8.1, 1.3$ Hz, 1H), 7.58 (dd, $J = 7.0, 1.3$ Hz, 1H), 7.53 – 7.47 (m, 1H), 7.39 (dd, $J = 8.3, 4.2$ Hz, 1H), 4.33 (s, 2H), 2.57 (t, $J = 7.4$ Hz, 2H), 1.62 – 1.56 (m, 2H), 1.32 – 1.23 (m, 22H), 0.88 (t, $J = 6.7$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 209.6, 149.7, 136.4, 134.5, 130.7, 128.6, 127.3, 126.4, 121.3, 45.6, 42.8, 32.1, 29.83, 29.79, 29.75, 29.62, 29.55, 29.5, 29.3, 24.0, 22.8, 14.3. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{38}\text{NO}$ 368.2948; found 368.2951.

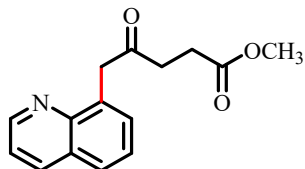


1-(benzyloxy)-3-(quinolin-8-yl)propan-2-one (6q). Colorless liquid. (45.5mg, 78%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.83 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.14 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.76 (dd, $J = 8.2, 1.1$ Hz, 1H), 7.60 (d, $J = 6.9$ Hz, 1H), 7.54 – 7.47 (m, 1H), 7.42 – 7.27 (m, 7H), 4.64 (s, 2H), 4.40 (s, 2H), 4.33 (s, 2H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 206.7, 149.7, 146.6, 137.6, 136.4, 133.8, 131.0, 128.6, 128.1, 128.0, 127.5, 126.5, 121.3, 75.1, 73.4, 42.2. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{17}\text{NO}_2\text{Na}$ 314.1151; found 314.1141.

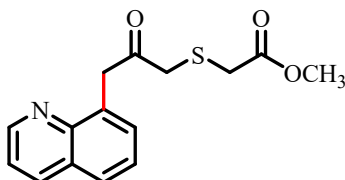


5-oxo-6-(quinolin-8-yl)hexanenitrile (6r) ^[10]. Colorless liquid. (41.0mg, 86%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.89 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.15 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.77 (dd, $J = 8.1, 1.4$ Hz, 1H), 7.61 – 7.54 (m, 1H), 7.53 – 7.46 (m, 1H), 7.41 (dd, $J = 8.3, 4.2$ Hz, 1H), 4.29 (s, 2H), 2.83 (t, $J = 6.7$ Hz, 2H), 2.40

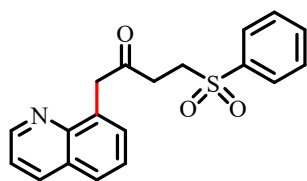
(t, $J = 7.0$ Hz, 2H), 1.94 (p, $J = 6.8$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.7, 149.9, 146.6, 136.4, 134.2, 130.8, 128.6, 127.6, 126.5, 121.4, 119.7, 46.0, 40.3, 19.7, 16.5.



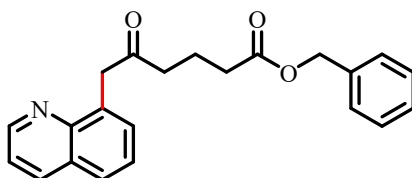
methyl 4-oxo-5-(quinolin-8-yl)pentanoate (6s). Colorless liquid. (36.0mg, 70%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.88 (dd, $J = 4.2, 1.8$ Hz, 1H), 8.14 (dd, $J = 8.3, 1.8$ Hz, 1H), 7.76 (dd, $J = 8.2, 1.4$ Hz, 1H), 7.64 – 7.57 (m, 1H), 7.51 (dd, $J = 8.1, 7.1$ Hz, 1H), 7.40 (dd, $J = 8.3, 4.2$ Hz, 1H), 4.37 (s, 2H), 3.64 (s, 3H), 2.93 (t, $J = 6.7$ Hz, 2H), 2.59 (t, $J = 6.7$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.4, 173.6, 149.8, 146.8, 136.4, 134.1, 130.9, 128.6, 127.5, 126.5, 121.3, 51.9, 45.6, 37.2, 28.1. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_3\text{Na}$ 280.0944; found 280.0937.



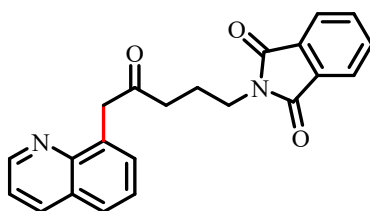
methyl 2-((2-oxo-3-(quinolin-8-yl)propyl)thio)acetate (6t). Light yellow liquid. (39.4mg, 68%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.86 (dd, $J = 4.2, 1.8$ Hz, 1H), 8.15 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.76 (dd, $J = 8.2, 1.4$ Hz, 1H), 7.62 (d, $J = 8.1$ Hz, 1H), 7.51 (dd, $J = 8.1, 7.1$ Hz, 1H), 7.40 (dd, $J = 8.3, 4.2$ Hz, 1H), 4.45 (s, 2H), 3.70 (s, 3H), 3.65 (s, 2H), 3.34 (s, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 203.4, 170.6, 149.8, 146.6, 136.4, 134.0, 131.0, 128.6, 127.6, 126.5, 121.4, 52.5, 44.15, 41.5, 33.3. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_3\text{SNa}$ 312.0665; found 312.0658.



1-(phenylsulfonyl)-3-(quinolin-8-yl)propan-2-one (6u). Light yellow liquid. (39.7mg, 61%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.80 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.15 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.88 – 7.82 (m, 2H), 7.76 (dd, $J = 8.1, 1.2$ Hz, 1H), 7.64 (t, $J = 7.5$ Hz, 1H), 7.57 – 7.44 (m, 4H), 7.40 (dd, $J = 8.3, 4.2$ Hz, 1H), 4.28 (s, 2H), 3.53 – 3.25 (t, 2H), 3.22 – 2.95 (t, 2H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 204.8, 149.9, 146.5, 139.1, 136.5, 133.9, 133.5, 130.9, 129.4, 128.6, 128.1, 127.8, 126.5, 121.4, 51.0, 45.8, 35.2. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{17}\text{NO}_3\text{SNa}$ 362.0821; found 362.0823.

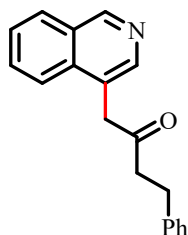


benzyl 5-oxo-6-(quinolin-8-yl)hexanoate (6v). Colorless liquid. (61.1mg, 88%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.84 (dd, $J = 4.2, 1.8$ Hz, 1H), 8.13 (dd, $J = 8.3, 1.8$ Hz, 1H), 7.75 (dd, $J = 8.1, 1.5$ Hz, 1H), 7.56 (dd, $J = 7.3, 1.0$ Hz, 1H), 7.49 (dd, $J = 8.0, 7.1$ Hz, 1H), 7.40 – 7.28 (m, 6H), 5.09 (s, 2H), 4.29 (s, 2H), 2.68 (t, $J = 7.1$ Hz, 2H), 2.39 (t, $J = 7.4$ Hz, 2H), 1.96 (p, $J = 7.2$ Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 208.4, 173.3, 149.8, 146.7, 136.3, 136.1, 134.3, 130.7, 128.7, 128.6, 128.3, 127.4, 126.4, 121.3, 66.2, 45.7, 41.4, 33.4, 19.1. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{21}\text{NO}_3\text{Na}$ 370.1414; found 370.1413.

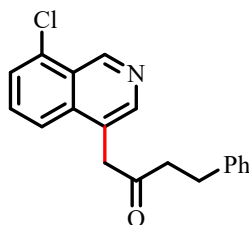


2-(4-oxo-5-(quinolin-8-yl)pentyl)isoindoline-1,3-dione (6w). Colorless solid. (61.6mg, 86%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.82 (dd, $J =$

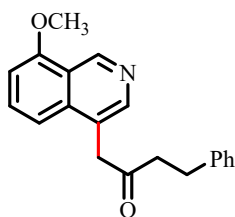
4.2, 1.8 Hz, 1H), 8.10 (dd, $J = 8.3, 1.8$ Hz, 1H), 7.81 (dd, $J = 5.4, 3.0$ Hz, 2H), 7.73 – 7.64 (m, 3H), 7.57 (dd, $J = 7.0, 1.2$ Hz, 1H), 7.51 – 7.42 (m, 1H), 7.39 – 7.29 (m, 1H), 4.31 (s, 2H), 3.68 (t, $J = 6.9$ Hz, 2H), 2.67 (t, $J = 7.3$ Hz, 2H), 1.98 (p, $J = 7.1$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.9, 168.5, 149.7, 146.7, 136.3, 134.2, 134.0, 132.2, 130.8, 128.5, 127.4, 126.4, 123.3, 121.2, 45.6, 39.6, 37.4, 22.9. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_3\text{Na}$ 381.1210; found 381.1201.



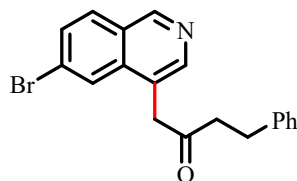
1-(isoquinolin-4-yl)-4-phenylbutan-2-one (7a) ^[10]. White solid. (28.1 mg, 51%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 9.19 (s, 1H), 8.37 (s, 1H), 7.99 (d, $J = 8.1$ Hz, 1H), 7.73 – 7.68 (m, 2H), 7.64 – 7.60 (m, 1H), 7.23 (t, $J = 7.3$ Hz, 2H), 7.18 – 7.14 (m, 1H), 7.09 (d, $J = 6.9$ Hz, 2H), 4.03 (s, 2H), 2.89 (dd, $J = 8.2, 5.3$ Hz, 2H), 2.80 (dd, $J = 8.4, 5.4$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.0, 152.6, 144.2, 140.7, 135.1, 131.1, 128.6, 128.4, 127.5, 126.3, 124.6, 123.3, 45.7, 43.4, 29.9.



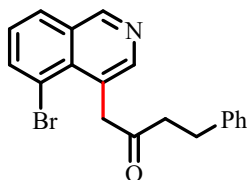
1-(8-chloroisoquinolin-4-yl)-4-phenylbutan-2-one (7b). Yellow solid. (35.3 mg, 57%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 9.62 (s, 1H), 8.43 (s, 1H), 7.63 (dd, $J = 6.8, 1.6$ Hz, 1H), 7.61 – 7.52 (m, 2H), 7.24 – 7.15 (m, 3H), 7.08 (d, $J = 6.8$ Hz, 2H), 4.03 (s, 2H), 2.88 (dd, $J = 8.2, 5.0$ Hz, 2H), 2.82 (dd, $J = 7.9, 4.7$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 206.5, 149.7, 145.3, 140.5, 136.5, 133.3, 130.8, 128.6, 128.4, 127.8, 126.4, 125.8, 124.2, 122.5, 45.7, 43.4, 29.9. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{17}\text{ClNO}$ 310.0993; found 310.0991.



1-(8-methoxyisoquinolin-4-yl)-4-phenylbutan-2-one (7c). Yellow solid. (42.8 mg, 70%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 9.10 (s, 1H), 8.18 (s, 1H), 7.55 (dd, $J = 8.1, 0.9$ Hz, 1H), 7.49 (t, $J = 7.9$ Hz, 1H), 7.26 (t, $J = 7.2$ Hz, 2H), 7.18 (t, $J = 8.6$ Hz, 3H), 6.96 (d, $J = 7.6$ Hz, 1H), 4.14 (s, 2H), 3.71 (s, 3H), 2.93 (t, $J = 7.4$ Hz, 2H), 2.79 (t, $J = 7.5$ Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 206.5, 155.5, 145.5, 141.3, 130.3, 128.6, 127.6, 126.2, 124.3, 120.7, 109.4, 55.2, 48.6, 43.6, 29.6. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{20}\text{NO}_2$ 306.1489; found 306.1491.

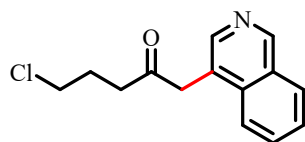


1-(6-bromoisoquinolin-4-yl)-4-phenylbutan-2-one (7d). Yellow solid. (34.7 mg, 49%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 9.13 (s, 1H), 8.35 (s, 1H), 7.90 (s, 1H), 7.83 (d, $J = 8.7$ Hz, 1H), 7.69 (dd, $J = 8.7, 1.7$ Hz, 1H), 7.27 – 7.21 (m, 2H), 7.17 (d, $J = 7.2$ Hz, 1H), 7.12 (d, $J = 8.1$ Hz, 2H), 3.98 (s, 2H), 2.91 (dd, $J = 8.1, 4.7$ Hz, 2H), 2.85 (dd, $J = 8.4, 4.8$ Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 206.2, 152.4, 145.2, 140.6, 136.2, 131.1, 130.0, 128.7, 128.4, 126.9, 126.4, 126.1, 125.9, 123.6, 45.2, 43.6, 29.9. **HRMS (ESI-TOF) m/z:** $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{17}\text{BrNO}$ 354.0488; found 354.0481.

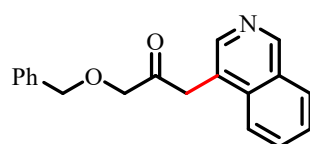


1-(5-bromoisoquinolin-4-yl)-4-phenylbutan-2-one (7e). Yellow solid. (32.6 mg, 46%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 9.17 (s, 1H), 8.23 (s, 1H), 7.96 (dd, $J = 7.8, 3.5$ Hz, 2H), 7.40 (t, $J = 7.8$ Hz, 1H), 7.32 – 7.27 (m, 2H), 7.21

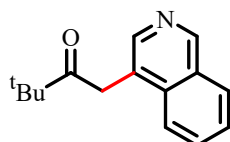
(d, $J = 6.5$ Hz, 3H), 4.52 (s, 2H), 2.98 (q, $J = 3.5$ Hz, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 206.5, 154.0, 148.2, 141.1, 137.6, 133.8, 130.8, 129.3, 128.7, 128.6, 127.6, 126.3, 124.3, 118.3, 47.9, 44.0, 29.9. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{17}\text{BrNO}$ 354.0488; found 354.0479.



5-chloro-1-(isoquinolin-4-yl)pentan-2-one (7g). Colorless liquid. (26.8 mg, 54%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 9.20 (s, 1H), 8.42 (s, 1H), 8.00 (d, $J = 8.1$ Hz, 1H), 7.83 (d, $J = 8.4$ Hz, 1H), 7.76 – 7.74 (m, 1H), 7.64 (td, $J = 7.0, 0.9$ Hz, 1H), 4.09 (s, 2H), 3.50 (t, $J = 6.3$ Hz, 2H), 2.70 (t, $J = 6.9$ Hz, 2H), 2.00 (p, $J = 6.7$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 206.6, 152.7, 144.2, 135.0, 131.1, 128.6, 128.5, 127.5, 124.5, 123.1, 45.3, 44.3, 38.5, 26.2. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{15}\text{ClNO}$ 248.0837; found 248.0835.

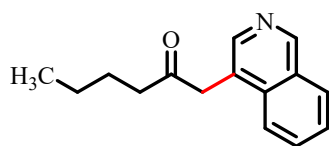


1-(benzyloxy)-3-(isoquinolin-4-yl)propan-2-one (7h). Colorless liquid. (29.1 mg, 50%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 9.19 (s, 1H), 8.39 (s, 1H), 8.01 (d, $J = 7.9$ Hz, 1H), 7.82 (d, $J = 8.4$ Hz, 1H), 7.74 – 7.69 (m, 1H), 7.62 (td, $J = 7.4, 0.9$ Hz, 1H), 7.38 – 7.30 (m, 5H), 4.59 (s, 2H), 4.20 (s, 2H), 4.16 (s, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.6, 152.6, 144.4, 137.0, 135.1, 131.0, 128.7, 128.6, 128.5, 128.3, 128.1, 127.4, 124.0, 123.3, 74.7, 73.7, 41.3. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{18}\text{NO}_2$ 292.1332; found 292.1326.

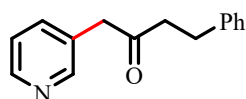


1-(isoquinolin-4-yl)-3,3-dimethylbutan-2-one (7j) ^[10]. Colorless liquid. (30.9 mg, 68%, 0.2 mmol scale); ^1H NMR (400 MHz, Chloroform-*d*) δ 9.16 (s, 1H), 8.30 (s, 1H), 7.97 (d, $J = 8.1$ Hz, 1H), 7.69 (dd, $J = 4.3, 1.0$ Hz, 2H), 7.59 (dt, $J = 8.1, 4.0$ Hz,

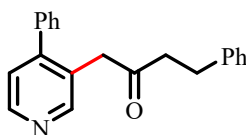
1H), 4.21 (s, 2H), 1.32 (s, 9H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 212.0, 152.3, 144.3, 135.4, 130.6, 128.6, 128.4, 127.1, 125.4, 123.3, 45.0, 38.3, 26.8.



1-(isoquinolin-4-yl)hexan-2-one (7i). Colorless liquid. (35.9 mg, 79%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 9.19 (s, 1H), 8.41 (s, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.75 – 7.71 (m, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 4.06 (s, 2H), 2.47 (t, *J* = 7.4 Hz, 2H), 1.53 (p, *J* = 7.5 Hz, 2H), 1.23 (dq, *J* = 14.7, 7.3 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 208.0, 152.6, 144.3, 135.1, 131.0, 128.6, 128.4, 127.4, 124.8, 123.3, 45.3, 41.7, 25.9, 22.3, 13.9. HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₅H₁₈NO 228.1383; found 228.1380.

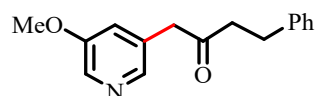


4-phenyl-1-(pyridin-3-yl)butan-2-one (8a). Light yellow liquid. (16.7 mg, 37%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.52 – 8.50 (m, 1H), 8.40 (d, *J* = 1.7 Hz, 1H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.29 – 7.18 (m, 5H), 7.15 (d, *J* = 6.8 Hz, 2H), 3.66 (s, 2H), 2.91 (t, *J* = 7.0 Hz, 2H), 2.84 – 2.81 (m, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 206.3, 150.5, 148.5, 140.7, 137.2, 129.8, 128.7, 128.5, 126.4, 123.6, 47.1, 44.1, 29.9. HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₅H₁₆NO 226.1226; found 226.1217.

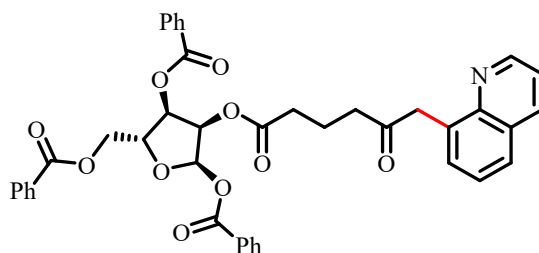


4-phenyl-1-(4-phenylpyridin-3-yl)butan-2-one (8b). Yellow liquid. (22.9 mg, 38%, 0.2 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.56 (d, *J* = 5.0 Hz, 1H), 8.42 (s, 1H), 7.41 (dd, *J* = 4.9, 1.7 Hz, 3H), 7.31 – 7.25 (m, 2H), 7.24 – 7.16 (m, 4H), 7.11 (d, *J* = 6.9 Hz, 2H), 3.69 (s, 2H), 2.80 (t, *J* = 7.5 Hz, 2H), 2.62 (t, *J* = 7.5 Hz, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 206.6, 151.9, 150.0, 140.8, 138.7, 128.7, 128.6,

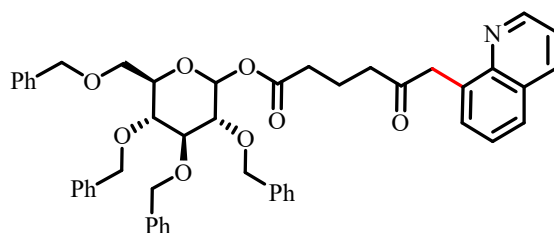
128.43, 128.37, 127.9, 126.3, 124.5, 44.9, 44.3, 29.7. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ calcd for $C_{21}H_{20}NO$ 302.1539; found 302.1541.



1-(5-methoxypyridin-3-yl)-4-phenylbutan-2-one (8c). Yellow liquid. (20.4 mg, 40%, 0.2 mmol scale); 1H NMR (400 MHz, Chloroform-*d*) δ 8.22 (d, $J = 2.8$ Hz, 1H), 8.02 (d, $J = 1.6$ Hz, 1H), 7.31 – 7.25 (m, 2H), 7.20 (t, $J = 7.3$ Hz, 1H), 7.15 (d, $J = 6.9$ Hz, 2H), 7.01 – 6.98 (m, 1H), 3.84 (s, 3H), 3.65 (s, 2H), 2.91 (t, $J = 7.0$ Hz, 2H), 2.86 – 2.79 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 206.3, 155.7, 142.6, 140.7, 136.5, 130.3, 128.6, 128.4, 126.4, 121.5, 55.6, 46.9, 44.0, 29.8. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ calcd for $C_{16}H_{18}NO_2$ 256.1332; found 256.1335.



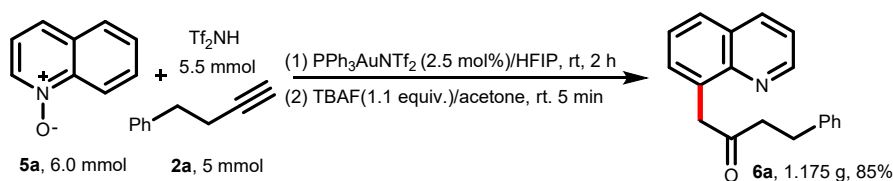
(2R,3R,4R,5R)-5-((benzoyloxy)methyl)-3-((5-oxo-6-(quinolin-8-yl)hexanoyl)oxy) tetrahydrofuran-2,4-diyl dibenzoate (13). Colorless liquid. (123.5mg, 88%, 0.2 mmol scale); 1H NMR (400 MHz, Chloroform-*d*) δ 8.77 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.11 – 8.08 (m, 6H), 7.72 (dd, $J = 7.4, 2.3$ Hz, 1H), 7.61 – 7.57 (m, 3H), 7.50 – 7.41 (m, 4H), 7.39 – 7.35 (m, 5H), 7.30 (dd, $J = 8.3, 4.2$ Hz, 1H), 6.80 (d, $J = 4.4$ Hz, 1H), 5.77 (dd, $J = 6.5, 2.1$ Hz, 1H), 5.55 (dd, $J = 6.4, 4.5$ Hz, 1H), 4.84 (q, $J = 3.1$ Hz, 1H), 4.71 (dd, $J = 12.2, 3.1$ Hz, 1H), 4.64 – 4.63 (m, 1H), 4.14 (s, 2H), 2.57 (t, $J = 7.0$ Hz, 2H), 2.32 (t, $J = 7.2$ Hz, 2H), 1.84 (p, $J = 7.1$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.0, 171.9, 166.2, 165.8, 165.3, 149.6, 146.6, 136.3, 134.2, 133.7, 133.6, 133.5, 130.7, 130.0, 129.9, 129.8, 129.6, 129.5, 129.2, 128.69, 128.66, 128.5, 128.4, 127.3, 126.3, 121.2, 94.8, 82.9, 70.80, 70.75, 64.1, 45.6, 41.1, 32.7, 18.6. **HRMS (ESI-TOF) m/z:** $[M + Na]^+$ calcd for $C_{41}H_{35}NO_{10}Na$ 724.2153; found 724.2159.



(3R,4S,5R,6R)-3,4,5-tris(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2H-pyran-2-yl 5-oxo-6-(quinolin-8-yl)hexanoate (14). Colorless liquid. (127.9mg, 82%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.87 (td, $J = 4.4, 1.7$ Hz, 1H), 8.17 – 8.13 (m, 1H), 7.75 – 7.70 (m, 1H), 7.51 (q, $J = 7.3$ Hz, 1H), 7.33 (dt, $J = 13.2, 5.8$ Hz, 20H), 7.18 – 7.17 (m, 2H), 6.44 (d, $J = 3.5$ Hz, 1H), 4.93 (dd, $J = 17.5, 10.9$ Hz, 1H), 4.87 – 4.71 (m, 3H), 4.67 – 4.58 (m, 2H), 4.52 (td, $J = 12.2, 3.1$ Hz, 2H), 4.28 (dd, $J = 11.6, 3.6$ Hz, 2H), 4.00 – 3.96 (m, 1H), 3.80 – 3.73 (m, 4H), 3.61 (dd, $J = 16.3, 7.9$ Hz, 1H), 2.72 (t, $J = 7.1$ Hz, 2H), 2.48 – 2.46 (m, 2H), 1.99 (dq, $J = 13.4, 7.0$ Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 208.22, 208.17, 171.84, 171.80, 149.7, 146.7, 138.7, 138.2, 138.1, 136.29, 136.25, 134.3, 130.71, 130.68, 128.6, 128.5, 128.2, 128.2, 128.0, 127.9, 127.84, 127.77, 127.71, 127.4, 127.3, 126.38, 126.35, 121.3, 121.2, 94.1, 90.0, 84.9, 81.8, 81.1, 79.0, 77.2, 75.8, 75.7, 75.6, 75.3, 75.1, 75.0, 73.61, 73.58, 73.2, 73.0, 68.2, 45.7, 41.3, 33.4, 19.0, 18.7. **HRMS (ESI-TOF) m/z :** $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{49}\text{H}_{49}\text{NO}_8\text{Na}$ 802.3350; found 802.3358.

6. A general procedure for Scheme 2

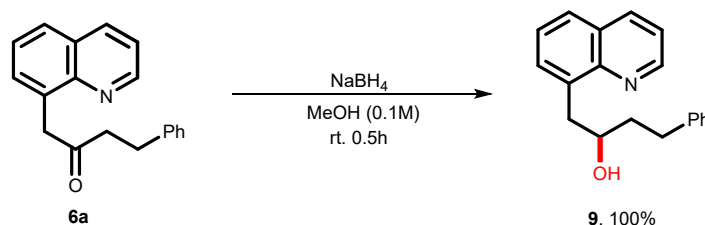
(A) Gram scale synthesis



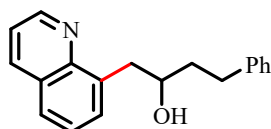
A solution of **5a** (0.87 g, 6.0 mmol, 1.2 eq.), HNTf₂ (1.55 g, 5.50 mmol, 1.1 eq.) in HFIP (12 mL) was stirred at room temperature for 15 min. The **2a** (0.65 g, 5.0 mmol) and PPh₃AuNTf₂ (92 mg, 125 μmol , 2.5 mol%) were added and stirred at room temperature for another 2 hours. Upon completion, the HFIP was removed under reduced pressure. TBAF (1.44 g, 5.50 mmol, 1.1 eq.) and acetone (25 mL) were then

added to the residue and stirred at room temperature for 5 min. The crude reaction mixture was then purified by column chromatography to afford the **6a** (1.175 g, 85% yield) as a white solid.

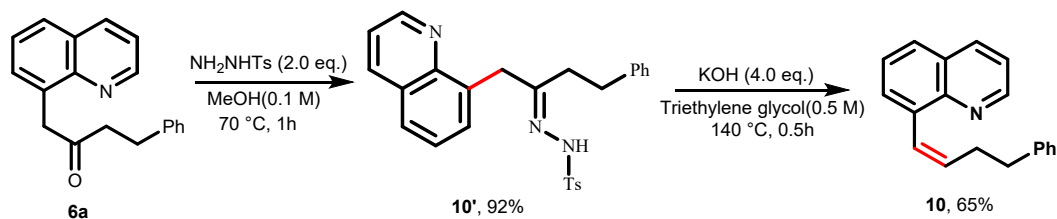
(B) Synthetic transformations



To a well stirred solution of **6a** (110.14 mg, 0.40 mmol) in MeOH (4.0 mL) at 0 °C was added NaBH₄ (16.65 mg, 0.44 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 1 h. Water (5 mL) was added to quench excess NaBH₄ and the mixture was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic extracts were then dried over Na₂SO₄ and conc. in vacuo. The residue was subjected to silica gel chromatography using Ethyl acetate and Petroleum ether (1:8) as eluents to afford the desired product **9** as a colorless liquid (110.95 mg, 100%).^[7]

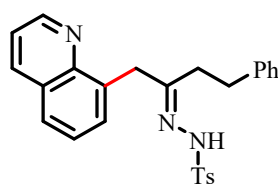


4-phenyl-1-(quinolin-8-yl)butan-2-ol (9). Colorless liquid. (110.95 mg, 100%, 0.4 mmol scale); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.88 (dd, *J* = 4.3, 1.8 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.73 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.55 (dd, *J* = 7.0, 1.2 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.44 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.30 – 7.22 (m, 4H), 7.17 (t, *J* = 7.0 Hz, 1H), 4.03 (dt, *J* = 11.6, 5.2 Hz, 1H), 3.44 (d, *J* = 5.0 Hz, 2H), 2.94 – 2.87 (m, 1H), 2.82 – 2.74 (m, 1H), 1.88 – 1.82 (m, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 149.2, 147.3, 142.8, 138.5, 137.4, 131.5, 128.9, 128.7, 128.4, 126.9, 126.8, 125.7, 121.2, 72.0, 41.5, 39.9, 32.5. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₉H₁₉NONa 300.1359; found 300.1357.



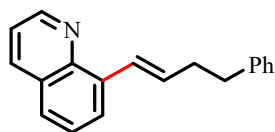
To a solution of **6a** (110.14 mg, 0.40 mmol) in MeOH (4.0 mL) were added NH_2NHTs (148.98 mg, 0.80 mmol), PTSA (4.13 mg, 0.024 mmol). The mixture was stirred at 70°C for 1 h. The organic solvent was removed under vacuum and the residue was dissolved in CH_2Cl_2 , washed with water (3×10 mL) and brine (3×10 mL), dried, filtered, and evaporated under reduced pressure. The crude reaction mixture was then purified by column chromatography using Ethyl acetate and Petroleum ether (1:4) as eluents to afford the **10'** (163 mg, 92%) as a white solid. [11]

KOH (44.88 mg, 0.8mmol) was added to triethylene glycol (0.5M) and heat to 100 °C until dissolved into a red/orange solution. **10'** (0.37 mmol) was added to the reaction system, and the reaction was heated at 140 °C for 0.5 hours. The reaction was cooled to room temperature, then diluted with water and extracted with ethyl acetate (3×5 mL). The combined organic extracts were then dried over Na_2SO_4 and conc. in vacuo. The crude product was purified by column chromatography to afford the **10** (62.37 mg, 65%) as a light yellow liquid.

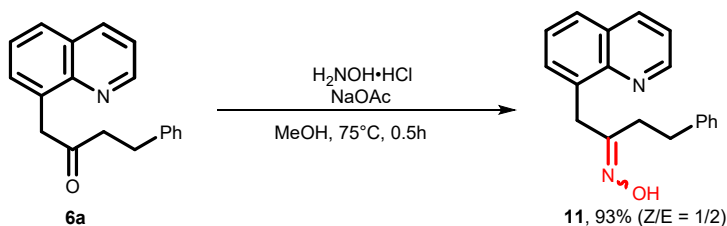


(E)-4-methyl-N'-(4-phenyl-1-(quinolin-8-yl)butan-2-ylidene)benzenesulfonohydrazide (10'). White solid. (163 mg, 92%, 0.4 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 12.98 (s, 1H), 9.01 (d, $J = 3.1$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H), 7.81 (d, $J = 7.9$ Hz, 2H), 7.75 (d, $J = 8.1$ Hz, 1H), 7.57 (d, $J = 6.8$ Hz, 1H), 7.52 (dd, $J = 8.1, 4.3$ Hz, 1H), 7.46 (t, $J = 7.5$ Hz, 1H), 7.12 (dt, $J = 17.4, 9.0$ Hz, 5H), 6.97 (d, $J = 6.9$ Hz, 2H), 3.99 (s, 2H), 2.79 – 2.75 (m, 2H), 2.57 – 2.53 (m, 2H), 2.31 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 156.5, 148.8, 145.0, 143.2, 141.8, 137.9, 136.4, 134.8, 131.9, 129.2, 128.8, 128.4, 128.3, 128.1, 127.6, 127.1, 125.9,

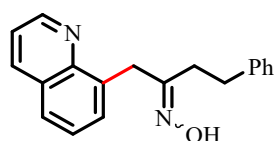
121.7, 37.5, 35.3, 31.9, 21.6. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ calcd for $C_{26}H_{26}N_3O_2S$ 444.1740; found 444.1732.



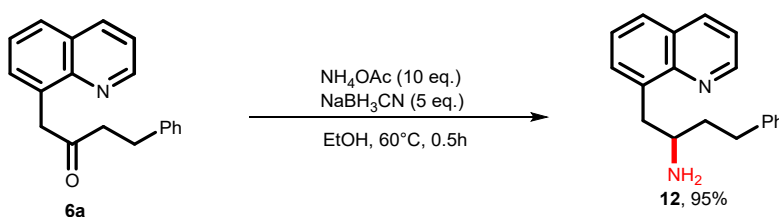
(E)-8-(4-phenylbut-1-en-1-yl)quinolone (10). Light yellow liquid. (62.37 mg, 65%); 1H NMR (400 MHz, Chloroform-*d*) δ 8.95 (dd, $J = 4.2, 1.8$ Hz, 1H), 8.14 (dd, $J = 8.3, 1.8$ Hz, 1H), 7.86 (d, $J = 7.2$ Hz, 1H), 7.74 – 7.66 (m, 2H), 7.54 – 7.48 (m, 1H), 7.41 (dd, $J = 8.3, 4.2$ Hz, 1H), 7.31 (dd, $J = 14.4, 7.4$ Hz, 5H), 7.21 (t, $J = 7.0$ Hz, 1H), 6.50 (dt, $J = 16.0, 6.9$ Hz, 1H), 2.95 – 2.84 (m, 2H), 2.71 (q, $J = 6.9$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.6, 145.8, 142.1, 136.6, 136.4, 132.6, 128.7, 128.6, 128.5, 126.9, 126.6, 126.3, 126.0, 125.5, 121.2, 36.2, 35.6. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ calcd for $C_{19}H_{18}N$ 260.1434; found 260.1433.



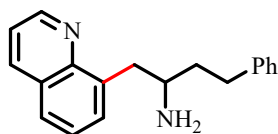
$H_2NOH \cdot HCl$ (16.68 mg, 0.24 mmol) and NaOAc (19.69 mg, 0.24 mmol) were added to a solution of the **6a** (55.07 mg, 0.2 mmol) in MeOH (2.0 mL). The mixture was heated at 75 °C for 12 h. After cooling to room temperature, the mixture was diluted with EtOAc (5 mL), washed with brine (5 mL), dried (Na_2SO_4) and concentrated in vacuo. The residue was subjected to silica gel chromatography using Ethyl acetate and Petroleum ether (1:5) as the eluent to provide the corresponding oxime **11** as a colorless liquid (54.0 mg, 93%).



4-phenyl-1-(quinolin-8-yl)butan-2-one oxime (11). Colorless liquid. (54.0 mg, 93%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.95 (dd, $J = 4.3, 1.8$ Hz, 1H), 8.20 (dd, $J = 8.3, 1.7$ Hz, 1H), 7.74 (td, $J = 8.3, 1.3$ Hz, 1H), 7.63 (dd, $J = 11.8, 7.1$ Hz, 1H), 7.53 – 7.36 (m, 2H), 7.22 (q, $J = 7.1$ Hz, 2H), 7.18 – 7.13 (m, 1H), 7.11 – 7.08 (m, 2H), 4.40 (s, 2H), 2.92 – 2.74 (m, 2H), 2.69 – 2.44 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 160.9, 149.4, 146.2, 141.7, 137.1, 135.2, 130.5, 128.6, 128.4, 127.1, 126.8, 126.4, 126.0, 121.4, 36.1, 32.8, 30.4. **HRMS (ESI-TOF) m/z:** [$\text{M} + \text{Na}$] $^+$ calcd for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_3\text{Na}$ 313.1311; found 313.1309.



6a (55.07 mg, 0.2 mmol), NH_4OAc (154.16 mg, 2 mmol), NaBH_3CN (62.84 mg, 1 mmol) were dissolved in ethanol (3 mL) and stir at 60 °C for 0.5 h. Dilute the reaction mixture with ethyl acetate. The organic layer is washed with 10% NaOH and salt water and dried with Na_2SO_4 . The organic layer is concentrated under reduced pressure. The residue was purified by silica gel column chromatography to provide the product **12** (52.5 mg, 95% yield) as a colorless liquid.^[12]



4-phenyl-1-(quinolin-8-yl)butan-2-amine (12). Colorless liquid. (52.5 mg, 95%, 0.2 mmol scale); $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.85 (dd, $J = 4.3, 1.7$ Hz, 1H), 8.20 (dd, $J = 8.3, 1.6$ Hz, 1H), 7.76 (d, $J = 8.0$ Hz, 1H), 7.53 (d, $J = 7.0$ Hz, 1H), 7.50 – 7.47 (m, 1H), 7.41 (dd, $J = 8.3, 4.4$ Hz, 1H), 7.20 – 7.16 (m, 2H), 7.11 (d, $J = 7.0$ Hz, 3H), 3.59 (dt, $J = 9.1, 4.7$ Hz, 1H), 3.55 – 3.42 (m, 2H), 2.81 – 2.69 (m, 2H), 2.08 – 2.00 (m, 1H), 1.93 – 1.85 (m, 1H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 149.5, 140.2, 138.3,

135.4, 132.6, 129.1, 128.7, 128.5, 128.1, 127.0, 126.3, 121.6, 52.2, 37.8, 35.2, 32.2.
HRMS (ESI-TOF) m/z: [M + H]⁺ calcd for C₁₉H₂₁N₂ 277.1699; found 277.1695.

7. Reference

- [1] A. T. Parsons, T. D. Senecal, S. L. Buchwald, *Angew. Chem. Int. Ed.*, 2012, **51**, 2947-2950.
- [2] Z. Lu, B. S. Bajwa, S. Liu, S. Lee, G. B. Hammond, B. Xu, *Green Chem.*, 2019, **21**, 1467-1471.
- [3] A. Groves, J. I. Martínez, J. J. Smith, H. W. Lam, *Chem. Eur. J.*, 2018, **24**, 13432-13436.
- [4] S. Yan, J. Rao, C.-Y. Zhou, *Org. Lett.*, 2020, **22**, 9091-9096.
- [5] Z. Xu, R. Zhai, T. Liang, L. Zhang, *Chem. Eur. J.*, 2017, **23**, 14133-14137.
- [6] W.-B. Zhang, X.-T. Yang, J.-B. Ma, Z.-M. Su, S.-L. Shi, *J. Am. Chem. Soc.*, 2019, **141**, 5628-5634.
- [7] Q. Liu, C.-S. Zhang, H. Sheng, D. Enders, Z.-X. Wang, X.-Y. Chen, *Org. Lett.*, 2020, **22**, 5617-5621..
- [8] G. A. Molander, L. Jean-Gérard, *J. Org. Chem.*, 2009, **74**, 1297-1303.
- [9] W. Huang, C. Wang, Y. Zhang, J. Qu, Y. Chen, *Org. Biomol. Chem.*, 2024, **22**, 2380-2383.
- [10] G. R. Mathi, B. Kweon, Y. Moon, Y. Jeong, S. Hong, *Angew. Chem. Int. Ed.*, 2020, **59**, 22675-22683.
- [11] G. Pazos, M. Pérez, Z. Gándara, G. Gómez, Y. Fall, *Tetrahedron*, 2012, **68**, 8994-9003.
- [12] E, J. Lavoie, H. Y. SAGONG, A. K. Parhi, Patent WO2019/99402A1, May, 23, 2019.

8. NMR spectra

