

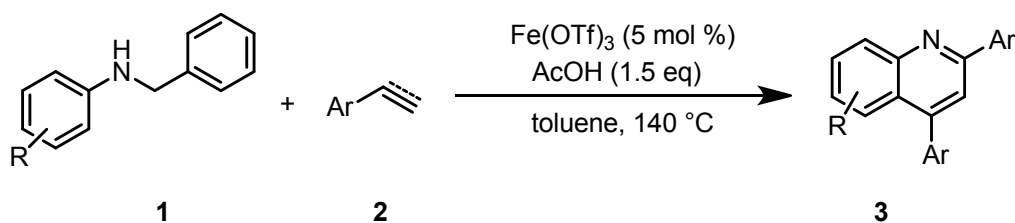
## Table of Contents

1. General Information .....	S2
2. Typical Procedure for Synthesis of 2,4-Diarylquinoline .....	S2
3. Gram-scale Synthesis .....	S8
4. Molecular Docking Studies .....	S8
5. Zebrafish Experiments .....	S9
6. NMR Spectra .....	S9

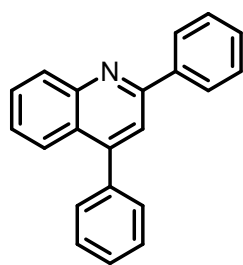
### 1. General Information

All reactions were conducted in pressure tubes under air. All solvents were received from commercial sources without further purification. Commercially available reagents were used as received. Non-commercially available substrates were synthesized following reported protocols. Thin-layer chromatography (TLC) was visualized using a combination of UV and potassium permanganate staining techniques. Silica gel (particle size 40 – 63  $\mu\text{m}$ ) was used for flash column chromatography. NMR spectra were recorded on Bruker AV 400 spectrometer at 400 MHz ( $^1\text{H}$  NMR), 100 MHz ( $^{13}\text{C}$  NMR). Proton and carbon chemical shifts are reported relative to the solvent used as an internal reference. High resolution mass spectra (HRMS) were recorded on Varian 7.0T FTICR LC/MS with Electron Spray Ionization (ESI) resource. The results of molecular docking experiments were completed using Schrödinger Suites.

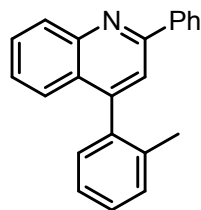
### 2. Typical Procedure for Synthesis of 2,4-Diarylquinoline



To a 15 mL pressure tube were added N-alkyl anilines **1** (0.2 mmol), Fe(OTf)<sub>3</sub> (5.0 mg, 5.0 μmol), AcOH (18 mg, 0.3 mmol), under air, and then alkenes or alkynes (0.4 mmol) and toluene (1 mL) were added. The resulting yellow solution was stirred at 140 °C for 24 h. After the reaction was completed, the solution was cooled to room temperature, and diluted with ethyl acetate and water (2 mL). The organic phase was separated and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in *vacuo*. The crude product was purified by column chromatography (*n*-Hex/EtOAc = 100:1 to 20:1) to afford the desired product.

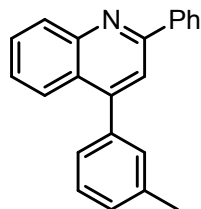


**3a**: 2,4-diphenylquinoline<sup>[1]</sup>. Colorless oil (46 mg, 82% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.25 (d, *J* = 4.0 Hz, 1H), 8.21 – 8.19 (m, 2H), 7.92 – 7.90 (m, 1H), 7.83 (s, 1H), 7.76 – 7.72 (m, 1H), 7.57 – 7.45 (m, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 157.1, 149.3, 149.0, 139.8, 138.6, 130.3, 129.5, 129.0, 128.7, 128.6, 127.7, 126.5, 125.9, 125.8, 119.5.

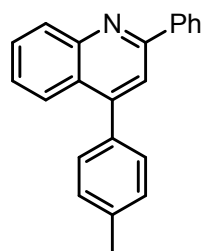


**3b**: 2-phenyl-4-(*o*-tolyl)quinoline<sup>[1]</sup>. Colorless oil (46 mg, 78% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.24 (d, *J* = 4.0 Hz, 1H), 8.21 – 8.19 (m, 2H), 7.77 (s, 1H), 7.74 –

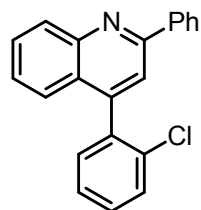
7.70 (m, 1H), 7.55 – 7.33 (m, 8H), 7.30 – 7.28 (m, 1H), 2.09 (m, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.1, 149.3, 148.7, 139.8, 138.0, 136.3, 130.4, 130.2, 129.8, 129.7, 129.5, 129.0, 128.6, 127.7, 126.5, 126.5, 126.0, 125.9, 119.6, 20.2.



**3c:** 2-phenyl-4-(*m*-tolyl) quinoline<sup>[2]</sup>. Colorless oil (48 mg, 81% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24 (d,  $J = 4.0$  Hz, 1H), 8.20 – 8.18 (m, 2H), 7.92 (d,  $J = 4.0$  Hz, 1H), 7.81 (s, 1H), 7.75 – 7.71 (m, 1H), 7.54 – 7.42 (m, 5H), 7.37 – 7.31 (m, 3H), 2.47 (m, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.0, 149.5, 148.9, 139.9, 138.5, 138.5, 130.4, 130.2, 129.6, 129.5, 129.3, 129.0, 128.6, 127.7, 126.8, 126.4, 126.0, 125.9, 119.5, 21.7.

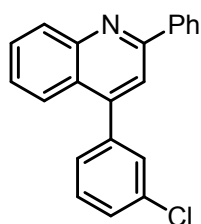


**3d:** 2-phenyl-4-(*p*-tolyl) quinoline<sup>[3]</sup>. Colorless oil (54 mg, 92% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.26 (d,  $J = 4.0$  Hz, 1H), 8.21 – 8.19 (m, 2H), 7.96 – 7.94 (m, 1H), 7.82 (s, 1H), 7.76 – 7.72 (m, 1H), 7.56 – 7.46 (m, 6H), 7.38 – 7.36 (m, 2H), 2.49 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.1, 149.4, 149.0, 139.9, 138.5, 135.6, 130.2, 129.6, 129.6, 129.4, 129.0, 127.7, 126.4, 126.0, 125.9, 119.5, 21.5.

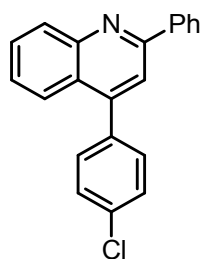


**3e:** 4-(2-chlorophenyl)-2-phenylquinoline<sup>[1]</sup>. Colorless oil (61 mg, 96% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (d,  $J = 4.0$  Hz, 1H), 8.21 – 8.19 (m, 2H), 7.81 (s, 1H), 7.76 – 7.71 (m, 1H), 7.60 – 7.58 (m, 1H), 7.55 – 7.39 (m, 8H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.0, 148.6, 146.7, 139.7, 137.2, 133.5, 132.0, 131.6, 131.3, 130.0, 130.0,

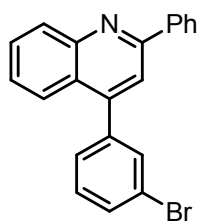
129.8, 129.6, 129.0, 127.8, 127.7, 126.6, 125.9, 125.7, 120.0.



**3f:** 4-(3-chlorophenyl)-2-phenylquinoline. Colorless oil (45 mg, 72% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (d,  $J = 4.0$  Hz, 1H), 8.20 – 8.18 (m, 2H), 7.85 (d,  $J = 4.0$  Hz, 1H), 7.80 (s, 1H), 7.77 – 7.73 (m, 1H), 7.57 – 7.43 (m, 8H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.0, 148.9, 147.7, 140.3, 139.6, 134.8, 130.4, 130.0, 129.9, 129.7, 129.6, 129.0, 128.7, 127.9, 127.7, 126.8, 125.6, 125.4, 119.4; HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{21}\text{H}_{14}\text{ClN}$   $[\text{M}+\text{H}]^+$  316.0893, Found 316.0882.

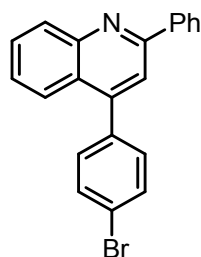


**3g:** 4-(4-chlorophenyl)-2-phenylquinoline<sup>[2]</sup>. Colorless oil (44 mg, 69% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24 (d,  $J = 4.0$  Hz, 1H), 8.20 – 8.18 (m, 2H), 7.95 – 7.93 (m, 1H), 7.81 (s, 1H), 7.75 – 7.71 (m, 1H), 7.55 – 7.45 (m, 6H), 7.38 – 7.36 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.1, 149.0, 148.0, 139.6, 137.0, 134.8, 131.0, 130.4, 129.8, 129.6, 129.0, 127.7, 126.7, 125.7, 125.4, 119.4.

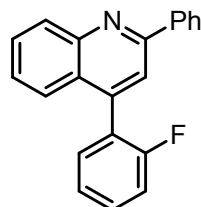


**3h:** 4-(3-bromophenyl)-2-phenylquinoline. Colorless oil (56 mg, 78% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (d,  $J = 4.0$  Hz, 1H), 8.19 – 8.17 (m, 2H), 7.84 (d,  $J = 4.0$  Hz, 1H), 7.78 (s, 1H), 7.76 – 7.72 (m, 1H), 7.69 – 7.67 (m, 2H), 7.55 – 7.42 (m, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.1, 149.0, 148.0, 139.6, 137.4, 132.0, 131.3, 130.4, 129.8, 129.6, 129.0, 127.7, 126.7, 125.6, 125.4, 123.0, 119.3; HRMS (ESI-

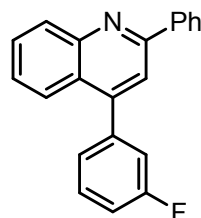
TOF)  $m/z$  Calcd for  $C_{21}H_{15}BrN$   $[M+H]^+$  360.0368, Found 360.0376.



**3i:** 4-(4-bromophenyl)-2-phenylquinoline<sup>[3]</sup>. Colorless oil (51 mg, 71% yield).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.25 (d,  $J = 4.0$  Hz, 1H), 8.20 – 8.18 (m, 2H), 7.85 (d,  $J = 4.0$  Hz, 1H), 7.79 (s, 1H), 7.77 – 7.73 (m, 1H), 7.55 – 7.46 (m, 8H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  157.0, 148.8, 147.9, 139.5, 137.3, 131.9, 131.2, 130.3, 129.7, 129.5, 128.9, 127.6, 126.6, 125.5, 125.3, 122.8, 119.2.

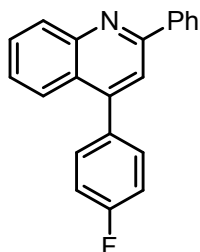


**3j:** 4-(2-fluorophenyl)-2-phenylquinoline. Colorless oil (37 mg, 61% yield).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.25 (d,  $J = 4.0$  Hz, 1H), 8.20 – 8.18 (m, 2H), 7.85 (s, 1H), 7.77 – 7.68 (m, 2H), 7.56 – 7.45 (m, 6H), 7.36 – 7.28 (m, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  161.1, 158.6, 157.0, 148.7, 143.4, 139.7, 131.9 (d,  $J_{C-F} = 3.0$  Hz), 130.7 (d,  $J_{C-F} = 4.0$  Hz), 130.3, 129.8, 129.6, 129.0, 127.8, 126.7, 126.0, 125.6, 124.5 (d,  $J_{C-F} = 2.0$  Hz), 120.4, 116.1 (d,  $J_{C-F} = 22.0$  Hz); HRMS (ESI-TOF)  $m/z$  Calcd for  $C_{21}H_{14}FN$   $[M+H]^+$  300.1189, Found 300.1179.

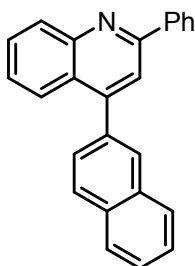


**3k:** 4-(3-fluorophenyl)-2-phenylquinoline. Colorless oil (35 mg, 59% yield).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.26 (d,  $J = 6.0$  Hz, 1H), 8.21 – 8.19 (m, 2H), 7.88 (d,  $J = 4.0$  Hz, 1H), 7.81 (s, 1H), 7.77 – 7.73 (m, 1H), 7.56 – 7.46 (m, 5H), 7.36 – 7.34 (m, 1H), 7.30 – 7.27 (m, 1H), 7.24 – 7.20 (m, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  164.2, 161.7,

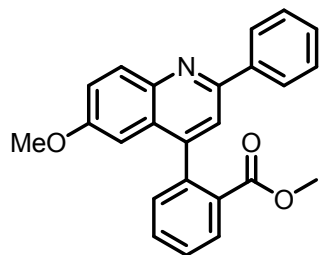
157.1, 149.0, 147.9, 140.7, 139.6, 130.4, 130.4, 130.3, 129.7 (d,  $J_{C-F} = 24.0$  Hz), 129.0, 127.7, 126.8, 125.6, 125.5 (d,  $J_{C-F} = 8.0$  Hz), 125.4, 119.4, 116.8 (d,  $J_{C-F} = 22.0$  Hz), 115.5 (d,  $J_{C-F} = 21.0$  Hz); HRMS (ESI-TOF)  $m/z$  Calcd for  $C_{21}H_{14}FN$   $[M+H]^+$  300.1189, Found 300.1179.



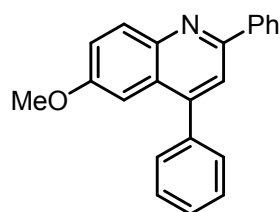
**3l:** 4-(4-fluorophenyl)-2-phenylquinoline<sup>[1]</sup>. Colorless oil (57 mg, 96% yield).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.25 (d,  $J = 4.0$  Hz, 1H), 8.21 – 8.18 (m, 2H), 7.87 – 7.85 (m, 1H), 7.80 (s, 1H), 7.74-7.73 (m, 1H), 7.56 – 7.46 (m, 6H), 7.28 – 7.23 (m, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  157.1, 149.0, 148.0, 139.6, 137.0, 134.8, 131.0, 130.4, 129.8, 129.6, 129.0, 127.7, 126.7, 125.7, 125.4, 119.4.



**3m:** 4-(naphthalen-2-yl)-2-phenylquinoline. Colorless oil (41 mg, 62% yield).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.28 (d,  $J = 4.0$  Hz, 1H), 8.23 – 8.20 (m, 2H), 8.05 – 8.01 (m, 2H), 7.98 – 7.92 (m, 4H), 7.78 – 7.73 (m, 1H), 7.70 – 7.68 (m, 1H), 7.61 – 7.45 (m, 6H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  157.0, 149.2, 148.8, 139.7, 135.9, 133.3, 133.0, 130.2, 129.6, 129.4, 128.9, 128.7, 128.2, 128.2, 127.8, 127.6, 127.4, 126.7, 126.7, 126.4, 125.9, 125.7, 119.7; HRMS (ESI-TOF)  $m/z$  Calcd for  $C_{25}H_{18}N$   $[M+H]^+$  332.1439, Found 332.1427.

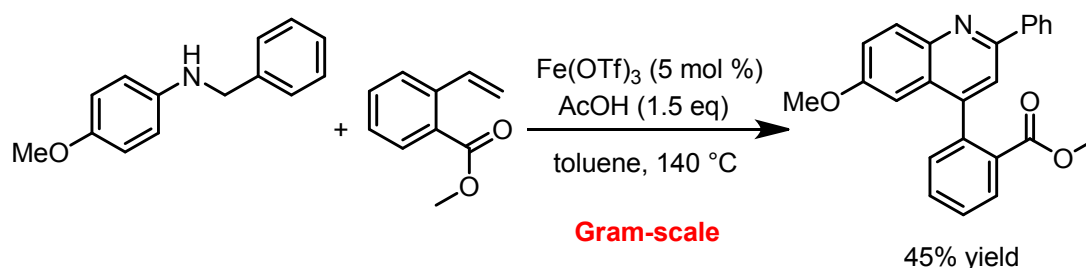


**3n:** methyl 2-(6-methoxy-2-phenylquinolin-4-yl)benzoate. Colorless oil (41 mg, 56% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.17 – 8.15 (m, 2H), 8.11 – 8.09 (m, 1H), 7.68 – 7.63 (m, 1H), 7.60 (s, 1H), 7.58 – 7.40 (m, 6H), 7.37 – 7.35 (m, 1H), 7.08 – 7.04 (m, 1H), 3.99 (s, 3H), 2.42 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  167.4, 160.6, 157.0, 149.9, 149.1, 139.8, 139.2, 132.0, 131.2, 130.9, 130.5, 129.2, 128.8, 128.5, 127.6, 126.3, 121.4, 119.4, 116.7, 107.9, 55.6, 52.0. HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{24}\text{H}_{19}\text{NO}_3$   $[\text{M}+\text{H}]^+$  370.1436, Found 370.1443.



**3o:** 6-methoxy-2,4-diphenylquinoline<sup>[1]</sup>. Colorless oil (49 mg, 79% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.17 – 8.14 (m, 3H), 7.78 (s, 1H), 7.60 – 7.50 (m, 7H), 7.46 – 7.39 (m, 2H), 7.20 (d,  $J = 2.0$  Hz, 1H), 3.81 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  157.8, 154.6, 147.9, 144.9, 139.7, 138.7, 131.6, 129.4, 129.0, 128.8, 128.7, 128.4, 127.3, 126.7, 121.8, 119.7, 103.7, 55.5.

### 3. Gram-scale Synthesis



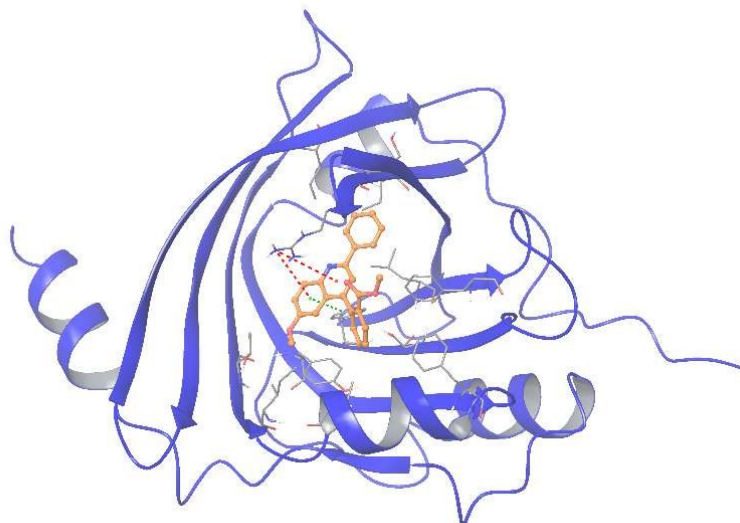
According to the typical procedure: To a 250 mL pressure tube were added *N*-benzyl-4-methoxyaniline (1.28 g, 6 mmol),  $\text{Fe}(\text{OTf})_3$  (150.9 mg, 300  $\mu\text{mol}$ ), and AcOH (720.6 mg, 12 mmol) under air. Then styrene (1.95 g, 12 mmol) and toluene

(50 mL) were added under air and this resulting yellow solution was stirred at 140 °C for 24 h. After column purification (*n*-Hex/EtOAc = 100:1 to 20:1), coupling product was obtained (1.0 g, 45% yield).

#### 4. Molecular Docking Studies

P02763:

Functions as transport protein in the blood stream. Binds various ligands in the interior of its beta-barrel domain. Also binds synthetic drugs and influences their distribution and availability in the body. Appears to function in modulating the activity of the immune system during the acute-phase reaction.



Green:  $\pi$ - $\pi$  interaction

Red:  $\pi$ -cation interaction

#### 5. Zebrafish Experiments

At 6 hpf, embryos were screened under anatomical microscope to remove the morphologically abnormal individuals. Around 10 healthy embryos were loaded into each well of 96-well plate in E3 solution. At the setting time, E3 solutions were replaced with different **3n** treatment solutions. The control and treated groups were analyzed at different intervals. At 55 hpf, the *Tg(fli1a:nEGFP)* zebrafish embryos were collected for imaging. At 55 hpf, for confocal imaging embryos were



anesthetized with E3/0.16 mg/mL tricaine/1% 1-phenyl-2-thiourea (Sigma) and embedded in 0.8% low melt agarose. Confocal imaging was performed with a Leica TCS-SP8 LSM. Analysis was performed using Imaris software.

## References

- [1]. J. Zhu, W. Hu, S. Sun, J.-T. Yu, J. Cheng, *Adv. Synth. Catal.* **2017**, 359, 3725.
- [2]. K. Sapkota, S.-S. Han, *New J. Chem.* **2017**, 41, 5395.
- [3]. Z. Zhang, H. Du, *Org. Lett.* **2015**, 17, 6266.

## 6. NMR Spectra

