Supporting Information

Rhodium-catalyzed synthesis of substituted isoquinolones via selective decarbonylation/alkyne insertion cascade of phthalimides

Fen Xu,*a Wen-Jing Zhu,a Juan Wang,b Qi Ma,a Li-Jing Shena

a Department of Material and Chemical Engineering, Zhengzhou University of Light Industry, Zhengzhou 450002, P. R. China.
b Henan Ecological and Environmental Monitoring Center, Zhengzhou 450002, P. R. China.

*E-mail: fenxu zzuli@163.com
Contents

1. General Information.................................................................S2

2. General Procedure...............................................................S2

3. Characterization of Phthalimides and Products .........................S3–S9

4. References..............................................................................S10

5. Single-Crystal X-Ray Crystallography.......................................S11–S12

6. Copy of NMR (\textsuperscript{1}H, \textsuperscript{13}C, \textsuperscript{19}F) Spectra............................................................S13–S66
1. General Information

Unless otherwise noted, all the reactions were carried out in a glassware under an air atmosphere. The commercially available chemicals and solvents were used as received without further purification. Phthalimides were prepared according to the published procedure. The reactions were monitored by TLC using UV-light or by staining with iodine. Column chromatography was performed on silica gel (200-300 mesh). Single-crystal X-ray data in this work were collected on an Agilent Technologies SuperNova Single Crystal Diffractometer at different temperatures equipped with graphite-monochromatic Mo Kα or Cu Kα radiation (λ = 0.71073 Å or 1.54184 Å). The structures were solved by SHELXS (direct methods) and refined by SHELXL (full matrix least-squares techniques) in the Olex2 package. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms attached to carbon were placed in geometrically idealized positions and refined using a riding model. 1H, 13C, and 19F NMR were recorded on a 400 MHz Bruker NMR spectrometer in CDCl₃ (7.26 ppm for 1H and 77.16 ppm for 13C) using tetramethylsilane (TMS) as the internal standard (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet).

2. General Procedure

A mixture of Rh(PPh₃)₂(CO)Cl (5 mol%), 2-(quinolin-8-yl)isoindoline-1,3-dione 1a (0.125 mmol), 1,2-diphenylethyne 2a (1.3 equiv), PhCl (2 mL) was reflux for 24 h. After cooling the reaction to room temperature, the solvent was removed under vacuum and the residue was purified by silica gel chromatography using petroleum ether/ethyl acetate = 10:1-4:1 to afford desired products 3aa-3ia and 3aa-3am.
3. Characterization of Phthalimides and Products

4-methyl-2-(quinolin-8-yl)isoindoline-1,3-dione (1c). white solid, mp 109.5-111.5°C. ‘H NMR (400 MHz, CDCl3) δ = 8.87 (dd, J=4.2, 1.7, 1H), 8.23 (dd, J=8.3, 1.7, 1H), 7.96 (dd, J=8.2, 1.5, 1H), 7.83 (d, J=7.3, 1H), 7.74 (dd, J=7.3, 1.5, 1H), 7.70 – 7.62 (m, 2H), 7.55 (d, J=7.7, 1H), 7.44 (dd, J=8.3, 4.2, 1H), 2.76 (s, 3H). ‘C NMR (101 MHz, CDCl3) δ = 168.7, 168.0, 151.0, 144.5, 138.6, 136.6, 136.2, 133.7, 132.9, 130.3, 130.0, 129.5, 129.3, 129.2, 126.2, 121.9, 121.5, 17.8.

3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3aa). white solid (93 %), mp 123.9-125.8°C. ‘H NMR (400 MHz, CDCl3) δ 8.93 (dd, J = 4.2, 1.6 Hz, 1H), 8.58 (dd, J = 7.9, 1.1 Hz, 1H), 8.05 (dd, J = 8.3, 1.5 Hz, 1H), 7.65 (dd, J = 8.2, 1.2 Hz, 1H), 7.63 – 7.56 (m, 1H), 7.56 – 7.46 (m, 2H), 7.41 – 7.33 (m, 2H), 7.31 (d, J = 8.0 Hz, 1H), 7.27 – 7.10 (m, 5H), 6.97 (d, J = 7.7 Hz, 1H), 6.82 (t, J = 7.2 Hz, 1H), 6.78 – 6.67 (m, 2H), 6.49 (dd, J = 11.0, 4.1 Hz, 1H). ‘C NMR (101 MHz, CDCl3) δ = 162.7, 150.7, 144.7, 141.8, 138.1, 137.7, 136.6, 136.0, 134.9, 132.4, 131.8, 131.7, 130.9, 130.8, 129.8, 128.7, 128.5, 128.4, 128.0, 127.8, 127.2, 126.7, 126.64, 126.62, 126.4, 125.8, 125.6, 125.6, 121.5, 118.5.

8-fluoro-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ba). white solid (88 %), mp164.5-165.9°C. ‘H NMR (400 MHz, CDCl3) δ = 8.92 (dd, J =4.2, 1.7, 1H), 8.43 (dd, J=8.0, 0.9, 1H), 8.03 (dd, J=8.3, 1.6, 1H), 7.64 (dd, J=8.2, 1.2, 1H), 7.47 (dd, J=11.4, 6.0, 3.0, 2H), 7.41 – 7.32 (m, 2H), 7.28 (ddd, J=12.2, 7.9, 1.3, 1H), 7.20 (ddd, J=8.3, 6.3, 4.6, 2H), 7.16 – 7.11 (m, 1H), 7.11 – 7.04 (m, 2H), 6.93 (d, J=7.6, 1H), 6.85 – 6.77 (m, 1H), 6.72 – 6.65 (m, 2H), 6.49 – 6.41 (m, 1H). ‘C NMR (101 MHz, CDCl3) δ = 161.67 (d, J = 3.1 Hz), 158.53 (d, J = 255.0 Hz), 150.8, 144.4, 143.2, 138.42 (d, J = 3.4 Hz), 137.4, 136.0, 134.4, 130.84 (dd, J = 13.5, 3.2 Hz), 130.8, 129.8, 128.71, 128.68, 127.80 (d, J = 2.5 Hz), 127.3, 127.2, 127.1, 126.75 (d, J = 9.0 Hz), 126.41 (d, J = 18.9 Hz), 126.3, 125.7, 124.61 (d, J = 3.9 Hz), 121.5, 119.45 (d, J = 22.3 Hz) 114.3.

8-methyl-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ca). white solid (51%), mp 161.2-162.7°C. ‘H NMR (400 MHz, CDCl3) δ = 8.91 (dd, J=4.2, 1.7, 1H), 8.56 (dd, J=5.8, 3.8, 1H), 8.02 (dd, J=8.3, 1.7, 1H), 7.62 (dd, J=8.2, 1.3, 1H), 7.47 (dd, J=7.3, 1.3, 1H), 7.44 – 7.39 (m, 2H), 7.37 – 7.31 (m, 2H), 7.21 – 7.13 (m, 2H), 7.12 – 7.00 (m, 3H), 6.90 (d, J=7.7, 1H), 6.78 (t, J=7.3, 1H), 6.69 – 6.59 (m, 2H), 6.42 (dd, J=7.6, 0.8, 1H), 1.82 (s, 3H). ‘C NMR (101 MHz, CDCl3) δ = 162.9, 150.7, 144.6, 142.5, 140.0, 137.8, 136.8, 136.0, 135.9, 135.3, 135.2, 132.3, 132.2, 131.1, 130.9, 130.0, 128.7, 128.5, 127.4, 127.3, 127.0, 126.9, 126.6, 126.5, 126.3, 126.1, 125.7, 121.5, 118.2, 112.0, 23.9.

8-chloro-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3da). white solid (42%), mp 164.4-166.1°C. ‘H NMR (400 MHz, CDCl3) δ =
6-chloro-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ea).
white solid (49%), mp 175.0-176.9°C. 1H NMR (400 MHz, CDCl₃) δ = 8.92 (dd, J=4.2, 1.7, 1H), 8.61 (dd, J=8.0, 1.5, 1H), 8.04 (dd, J=8.3, 1.7, 1H), 7.66 (dd, J=14.1, 8.0, 1.4, 2H), 7.50 – 7.40 (m, 2H), 7.40 – 7.31 (m, 2H), 7.15 (dt, J=7.4, 3.3, 2H), 7.11 – 6.98 (m, 3H), 6.91 (d, J=7.7, 1H), 6.80 (dd, J=11.0, 4.1, 1H), 6.67 (tdd, J=3.6, 2.2, 1.2, 2H), 6.46 – 6.38 (m, 1H). 13C NMR (101 MHz, CDCl₃) δ = 162.2, 150.8, 144.4, 144.1, 138.3, 137.4, 136.3, 136.0, 134.7, 134.3, 132.3, 132.2, 131.1, 130.9, 130.8, 129.8, 128.7, 128.7, 128.4, 128.1, 127.2, 127.1, 127.0, 127.0, 126.4, 126.40, 126.25, 125.7, 121.6, 116.6.

7-chloro-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ea’).
white solid (41%), mp 121.5-123.3°C. 1H NMR (400 MHz, CDCl₃) δ = 8.92 (dd, J=4.2, 1.7, 1H), 8.54 (d, J=2.3, 1H), 8.06 (dd, J=8.3, 1.7, 1H), 7.67 (dd, J=8.2, 1.3, 1H), 7.53 (dd, J=8.7, 2.3, 1H), 7.48 (dd, J=7.3, 1.3, 1H), 7.42 – 7.33 (m, 2H), 7.27 – 7.19 (m, 3H), 7.19 – 7.12 (m, 3H), 6.96 (d, J=7.7, 1H), 6.83 (t, J=7.5, 1H), 6.77 – 6.66 (m, 2H), 6.49 (dd, J=11.1, 4.1, 1H). 13C NMR (101 MHz, CDCl₃) δ = 161.7, 150.8, 144.6, 142.2, 137.4, 136.6, 136.1, 136.0, 134.6, 132.8, 132.7, 131.8, 131.5, 130.8, 130.7, 129.7, 128.8, 128.7, 128.1, 127.9, 127.8, 127.4, 127.4, 127.0, 126.7, 126.7, 126.5, 125.8, 121.6, 118.1.

6,7-dichloro-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3fa). white solid (32%), mp 154.7-156.4°C. 1H NMR (400 MHz, CDCl₃) δ = 8.92 (dd, J=4.2, 1.7, 1H), 8.63 (s, 1H), 8.06 (dd, J=8.3, 1.6, 1H), 7.67 (dd, J=8.2, 1.3, 1H), 7.47 (dd, J=7.3, 1.3, 1H), 7.42 – 7.34 (m, 3H), 7.29 – 7.22 (m, 1H), 7.22 – 7.09 (m, 4H), 6.95 (d, J=7.7, 1H), 6.84 (td, J=7.6, 0.7, 1H), 6.72 (ddd, J=21.7, 10.9, 4.5, 2H), 6.53 – 6.44 (m, 1H). 13C NMR (101 MHz, CDCl₃) δ = 161.2, 150.9, 144.5, 143.6, 137.7, 137.4, 137.2, 136.1, 135.5, 134.4, 131.7, 131.4, 131.1, 130.7, 130.5, 130.1, 129.5, 128.8, 128.8, 128.3, 128.1, 127.5, 127.2, 126.8, 126.5, 125.7, 125.0, 121.6, 117.2.

6-methyl-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ga’).
white solid (46%), mp 155.6-157.5°C. 1H NMR (400 MHz, CDCl₃) δ = 8.92 (dd, J=4.2, 1.7, 1H), 8.47 (d, J=8.2, 1H), 8.04 (dd, J=8.3, 1.7, 1H), 7.65 (dd, J=8.2, 1.3, 1H), 7.49 (dd, J=7.3, 1.3, 1H), 7.40 – 7.31 (m, 3H), 7.29 – 7.20 (m, 3H), 7.21 – 7.10 (m, 3H), 6.95 (d, J=7.7, 1H), 6.82 (t, J=7.2, 1H), 6.76 – 6.66 (m, 2H), 6.47 (td, J=7.6, 0.8, 1H), 2.39 (s, 3H). 13C NMR (101 MHz, CDCl₃) δ = 162.7, 150.7, 144.8, 143.0, 141.9, 138.2, 137.8, 136.7, 135.9, 135.0, 131.9, 131.7, 130.9, 130.8, 129.8, 128.7, 128.5, 128.3, 128.0, 127.7, 127.1, 126.7, 126.6, 126.4, 125.7, 125.3, 123.4, 121.4, 118.4, 22.1.
7-methyl-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ga).
white solid (50%), mp 160.7-162.5°C. 1H NMR (400 MHz, CDCl3) δ = 8.92 (dd, J = 4.2, 1.7, 1H), 8.38 (s, 1H), 8.05 (dd, J = 8.3, 1.7, 1H), 7.65 (dd, J = 8.2, 1.2, 1H), 7.48 (dd, J = 7.3, 1.3, 1H), 7.42 (dd, J = 8.3, 1.7, 1H), 7.39 – 7.32 (m, 2H), 7.25 – 7.18 (m, 3H), 7.18 – 7.10 (m, 3H), 6.96 (d, J = 7.7, 1H), 6.82 (t, J = 7.5, 1H), 6.71 (td, J = 7.6, 1.1, 2H), 6.48 (dt, J = 7.6, 3.8, 1H), 2.50 (s, 3H). 13C NMR (101 MHz, CDCl3) δ = 162.7, 150.7, 144.8, 140.9, 137.9, 136.8, 136.7, 136.0, 135.9, 135.0, 133.9, 131.9, 131.7, 130.9, 129.9, 128.7, 128.5, 128.0, 128.0, 127.7, 127.1, 126.7, 126.6, 126.4, 125.7, 125.6, 125.5, 121.4, 118.5, 21.4.

7-fluoro-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ha).
white solid (44%), mp 119.5-121.2°C. 1H NMR (400 MHz, CDCl3) δ 8.93 (dd, J = 4.2, 1.6 Hz, 1H), 8.29 – 8.14 (m, 1H), 8.06 (dd, J = 8.3, 1.4 Hz, 1H), 7.67 (dd, J = 8.2, 1.2 Hz, 1H), 7.49 (dd, J = 7.3, 1.2 Hz, 1H), 7.41 – 7.28 (m, 4H), 7.25 – 7.20 (m, 2H), 7.19 – 7.08 (m, 3H), 6.96 (d, J = 7.6 Hz, 1H), 6.82 (dd, J = 11.7, 4.2 Hz, 1H), 6.78 – 6.67 (m, 2H), 6.48 (dd, J = 11.0, 4.2 Hz, 1H). 13C NMR (101 MHz, CDCl3) δ = 161.87 (d, J = 3.5 Hz), 161.50 (d, J = 247.4 Hz), 150.8, 144.5, 141.1, 137.4, 136.3, 136.1, 134.79 (d, J = 2.1 Hz), 134.6, 131.64 (d, J = 21.3 Hz), 130.8, 129.8, 128.74, 128.68, 128.23 (d, J = 7.7 Hz), 127.99 (d, J = 24.5 Hz), 127.3, 127.18 (d, J = 8.1 Hz), 126.9, 126.57 (d, J = 22.7 Hz), 125.8, 121.5, 121.00 (d, J = 23.3 Hz), 118.1, 113.39 (d, J = 22.8 Hz). 19F NMR (376 MHz, CDCl3) δ = -113.79.

6-fluoro-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ha').
white solid (37%), mp 170.2-171.9°C. 1H NMR (400 MHz, CDCl3) δ 8.94 (dd, J = 4.2, 1.7 Hz, 1H), 8.58 (dd, J = 8.9, 6.0 Hz, 1H), 8.06 (dd, J = 8.3, 1.6 Hz, 1H), 7.67 (dd, J = 8.2, 1.3 Hz, 1H), 7.49 (dd, J = 7.3, 1.3 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.26 – 7.10 (m, 6H), 6.99 – 6.89 (m, 2H), 6.83 (dd, J = 11.8, 4.3 Hz, 1H), 6.73 (td, J = 7.4, 1.3 Hz, 2H), 6.53 – 6.44 (m, 1H). 13C NMR (101 MHz, CDCl3) δ = 165.59 (d, J = 251.7 Hz), 162.0, 150.8, 144.6, 143.2, 140.68 (d, J = 10.1 Hz), 137.4, 136.1, 136.0, 134.6, 131.67 (d, J = 10.0 Hz), 131.58 (d, J = 22.5 Hz), 131.58 (d, J = 22.5 Hz), 130.9, 130.6, 129.6, 128.7, 128.7, 128.08 (d, J = 22.7 Hz), 127.19 (d, J = 35.2 Hz), 126.58 (d, J = 22.5 Hz), 125.8, 122.2, 121.5, 118.04 (d, J = 3.2 Hz), 115.19 (d, J = 23.5 Hz), 110.82 (d, J = 23.2 Hz).

6,7-difluoro-3,4-diphenyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3la).
white solid (24%), mp 105.9-107.8°C. 1H NMR (400 MHz, CDCl3) δ = 8.93 (dd, J = 4.2, 1.7, 1H), 8.33 (dd, J = 10.7, 8.3, 1H), 8.07 (dd, J = 8.3, 1.6, 1H), 7.67 (dd, J = 8.2, 1.3, 1H), 7.48 (dd, J = 7.3, 1.4, 1H), 7.44 – 7.35 (m, 2H), 7.29 – 7.22 (m, 1H), 7.22 – 7.12 (m, 4H), 7.06 (dd, J = 11.7, 7.5, 1H), 6.95 (d, J = 7.7, 1H), 6.84 (t, J = 7.2, 1H), 6.77 – 6.68 (m, 2H), 6.52 – 6.43 (m, 1H). 19F NMR (376 MHz, CDCl3) δ = -129.40 (d, J = 22.0 Hz), -137.59 (d, J = 22.0 Hz). 13C NMR (101 MHz, CDCl3) δ = 161.28 (d, J = 3.7 Hz), 153.96 (dd, J = 255.1, 14.1 Hz), 150.84, 149.84 (dd, J = 250.9, 14.2 Hz), 144.49, 142.68 (d, J = 2.2 Hz), 137.26, 136.27 (d, J = 2.7 Hz), 136.19 (d, J = 2.5 Hz), 136.11, 135.87, 134.43, 131.49 (d, J = 25.2 Hz), 130.76, 130.11 (d, J = 99.2 Hz), 128.80, 128.78, 128.20 (d, J = 21.7 Hz), 127.34 (d, J = 26.3 Hz), 126.64 (d, J = 23.0 Hz), 124.59 (d, J = 23.0 Hz), 118.04 (d, J = 3.2 Hz).
125.76, 122.64 (dd, J = 6.2, 2.0 Hz), 121.61, 117.58, 116.46 (dd, J = 18.7, 1.9 Hz), 113.48 (d, J = 19.2 Hz).

2-(quinolin-8-yl)-3,4-di-p-tolylisoquinolin-1(2H)-one (3ab). white solid (95 %), mp 173.1-174.9°C. ¹H NMR (400 MHz, CDCl₃) δ = 8.91 (dd, J=4.2, 1.7, 1H), 8.56 (dd, J=7.9, 1.1, 1H), 7.63 (dd, J=8.2, 1.3, 1H), 7.60 – 7.53 (m, 1H), 7.52 – 7.42 (m, 2H), 7.39 – 7.27 (m, 3H), 7.13 (dd, J=7.9, 1.6, 1H), 7.04 (dd, J=7.9, 1.7, 2H), 6.96 (d, J=8.0, 1H), 6.84 (dd, J=7.8, 1.7, 1H), 6.66 – 6.57 (m, 2H), 6.27 (d, J=8.0, 1H), 2.25 (s, 3H), 1.92 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ = 162.8, 150.7, 144.8, 142.0, 138.5, 137.9, 136.7, 136.1, 136.0, 133.7, 132.3, 132.1, 131.7, 131.5, 130.8, 130.7, 129.6, 128.8, 128.7, 128.5, 128.4, 128.3, 127.4, 127.2, 126.5, 125.8, 125.7, 125.6, 121.4, 118.5, 21.2, 21.0.

3,4-bis(4-ethylphenyl)-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ac). white solid (97%), mp 143.9-145.7°C. ¹H NMR (400 MHz, CDCl₃) δ = 8.93 (dd, J = 4.2, 1.7 Hz, 1H), 8.57 (dd, J = 8.0, 1.1 Hz, 1H), 8.05 (dd, J = 8.3, 1.4 Hz, 1H), 7.69 – 7.54 (m, 2H), 7.54 – 7.42 (m, 2H), 7.40 – 7.29 (m, 3H), 7.15 (dd, J = 7.8, 1.7 Hz, 1H), 7.09 – 7.01 (m, 2H), 6.98 (dd, J = 7.9, 1.5 Hz, 1H), 6.84 (dd, J = 7.8, 1.7 Hz, 1H), 6.63 (td, J = 7.8, 1.3 Hz, 2H), 6.29 (dd, J = 7.9, 1.4 Hz, 1H), 2.56 (q, J = 7.6 Hz, 2H), 2.23 (q, J = 7.6 Hz, 2H), 1.17 (t, J = 7.6 Hz, 3H), 0.88 (dd, J = 9.1, 6.0 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ = 162.8, 150.6, 144.7, 142.9, 142.4, 142.0, 138.4, 137.9, 136.0, 133.8, 132.3, 131.7, 131.5, 130.8, 130.7, 129.7, 128.7, 128.3, 127.4, 127.1, 126.4, 126.0, 125.8, 125.8, 125.7, 125.5, 121.4, 118.5, 28.5, 28.2, 21.5, 15.0.

3,4-bis(4-fluorophenyl)-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ad). white solid (89 %), mp 152.5-154.2°C. ¹H NMR (400 MHz, CDCl₃) δ = 8.91 (dd, J = 4.2, 1.6 Hz, 1H), 8.58 (dd, J = 8.0, 1.1 Hz, 1H), 8.09 (d, J = 8.2 Hz, 1H), 7.71 (dd, J = 8.2, 1.2 Hz, 1H), 7.66 – 7.58 (m, 1H), 7.53 (ddd, J = 15.1, 7.9, 1.2 Hz, 2H), 7.45 – 7.33 (m, 2H), 7.27 (d, J = 6.7 Hz, 1H), 7.20 – 7.11 (m, 2H), 6.99 – 6.84 (m, 3H), 6.79 – 6.71 (m, 1H), 6.55 (td, J = 8.6, 2.7 Hz, 1H), 6.21 (td, J = 8.6, 2.7 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ = 162.68, 161.66 (d, J = 246.4 Hz), 161.44 (d, J = 248.0 Hz), 150.70, 144.41, 141.11, 137.93, 137.37, 136.28, 132.62, 130.93, 133.24 (dd, J = 27.8, 8.0 Hz), 132.30 (d, J = 3.5 Hz), 132.01 (dd, J = 76.8, 8.3 Hz), 130.85 (d, J = 3.6 Hz), 130.85 (d, J = 3.6 Hz), 128.85, 125.90, 125.67, 128.65 (d, J = 30.1 Hz), 126.94, 125.43, 115.11 (d, J = 3.4 Hz), 115.11 (d, J = 39.3 Hz), 113.83, 113.8 (d, J = 42.8 Hz). ¹⁹F NMR (376 MHz, CDCl₃) δ = -113.24, -115.05.

3,4-bis(4-chlorophenyl)-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ae). white solid (87%), mp 174.4-175.8°C. ¹H NMR (400 MHz, CDCl₃) δ = 8.90 (dd, J = 4.2, 1.6 Hz, 1H), 8.57 (dd, J = 8.0, 1.1 Hz, 1H), 8.08 (dd, J = 8.3, 1.5 Hz, 1H), 7.71 (dd, J = 8.2, 1.2 Hz, 1H), 7.65 – 7.57 (m, 1H), 7.57 – 7.47 (m, 2H), 7.44 – 7.32 (m, 2H), 7.28 – 7.07 (m, 6H), 6.87 (ddd, J = 24.1, 8.2, 2.1 Hz, 2H), 6.70 (dd, J = 8.3, 1.8 Hz, 1H), 6.50 (dd, J = 8.3, 2.1 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ = 162.6, 150.8, 144.4, 140.8, 137.6, 137.2, 136.2, 134.8, 133.4.
3,4-bis(4-bromophenyl)-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3af).
white solid (83%), mp 176.3-178.2°C. 1H NMR (400 MHz, CDCl3) δ = 8.91 (dd, J=4.2, 1.5, 1H), 8.56 (dd, J=7.9, 1.0, 1H), 8.11 (d, J=7.5, 1H), 7.73 (dd, J=8.2, 1.2, 1H), 7.66 – 7.58 (m, 1H), 7.58 – 7.47 (m, 2H), 7.46 – 7.32 (m, 4H), 7.24 (d, J=7.7, 1H), 7.08 (dd, J=7.5, 5.3, 1.9, 2H), 7.00 (d, J=8.3, 1H), 6.84 (d, J=8.2, 1H), 6.66 (s, 2H). 13C NMR (101 MHz, CDCl3) δ = 162.6, 150.8, 144.5, 140.7, 137.8, 137.2, 136.2, 135.3, 133.6, 133.4, 133.2, 132.7, 132.1, 131.5, 131.3, 130.8, 130.1, 129.9, 129.0, 128.8, 128.5, 127.1, 125.9, 125.7, 125.4, 121.8, 121.7, 121.3, 117.4.

3,4-bis(3-fluorophenyl)-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ag).
white solid (86%), mp 136.0-137.8°C. 1H NMR (400 MHz, CDCl3) δ = 8.96 – 8.86 (m, 1H), 8.58 (dd, J=8.0, 1.0, 1H), 8.07 (dd, J=8.1, 3.6, 1H), 7.69 (d, J=8.2, 1H), 7.66 – 7.58 (m, 1H), 7.58 – 7.48 (m, 2H), 7.45 – 7.34 (m, 2H), 7.30 – 7.11 (m, 2H), 7.06 – 6.74 (m, 4H), 6.73 – 6.54 (m, 1H), 6.49 (dd, J=21.8, 9.3, 4.6, 2H). 13C NMR (101 MHz, CDCl3) δ = 162.43 (dd, J= 246.3, 11.9, 3.3 Hz), 161.15 (ddd, J= 246.4, 13.8, 3.4 Hz), 162.54, 150.93 (d, J = 4.8 Hz), 150.77 (d, J = 4.9 Hz), 144.54, 144.50, 140.57, 138.46 (ddd, J = 7.4, 5.2, 2.1 Hz), 137.50, 137.21 (d, J = 1.5 Hz), 136.49 (dd, J = 11.4, 6.0 Hz), 136.15, 132.70, 130.88, 130.83, 130.77, 129.77, 129.69, 129.54 (dd, J = 10.6, 2.0 Hz), 129.39, 128.91, 128.85, 128.82, 128.54, 128.44, 128.34 (d, J = 1.9 Hz), 128.27 (d, J = 4.6 Hz), 128.20 (d, J = 2.2 Hz), 128.11, 127.63, 127.60, 127.57, 127.40 (dd, J = 2.7, 1.2 Hz), 127.11, 126.58 (d, J = 2.4 Hz), 125.90 (d, J = 5.0 Hz), 125.77 (d, J = 3.4 Hz), 125.72 (d, J = 2.8 Hz), 125.41, 121.73 (d, J = 2.6 Hz), 118.77 (d, J = 2.0 Hz), 118.55, 118.34, 117.64 (d, J = 22.0 Hz), 117.46 (d, J = 1.8 Hz), 117.44, 117.42, 116.91 (d, J = 22.6 Hz), 114.35 (ddd, J = 24.1, 21.0, 3.9 Hz). 19F NMR (376 MHz, CDCl3) δ = -113.34 (dd, J=104.7, 101.2), -114.00 (dd, J=108.6, 14.0).

3,4-bis(3-chlorophenyl)-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3ah).
white solid (85%), mp 153.5-155.2°C. 1H NMR (400 MHz, CDCl3) δ = 9.02 – 8.81 (m, 1H), 8.58 (d, J=7.9, 1H), 8.18 – 7.97 (m, 1H), 7.71 (d, J=8.2, 1H), 7.65 (dd, J=11.1.4, 0.0, 1H), 7.60 – 7.34 (m, 4H), 7.29 – 7.24 (m, 2H), 7.14 (m, J=17.6, 16.0, 9.5, 5.1, 3H), 7.04 – 6.70 (m, 3H), 6.51 (ddd, J=41.1, 15.8, 7.8, 1H). 13C NMR (101 MHz, CDCl3) δ = 162.54 (d, J = 2.5 Hz), 150.92 (d, J = 4.1 Hz), 150.75 (d, J = 4.8 Hz), 144.46, 140.68, 140.64, 140.55, 138.04, 137.45, 137.18, 137.09, 136.23, 136.14, 136.13, 136.09, 136.05, 133.92 (dd, J = 19.1, 16.6 Hz), 132.76, 132.57 (d, J = 3.2 Hz), 131.67 (d, J = 20.1 Hz), 131.59 (d, J = 21.2 Hz), 130.96, 130.72 (d, J = 3.8 Hz), 130.62 (d, J = 8.5 Hz), 130.09, 130.06, 129.97, 129.80 (d, J = 7.5 Hz), 129.58, 129.39 (d, J = 4.0 Hz), 129.22, 128.96 (d, J = 7.0 Hz), 128.88, 128.86, 128.75 (d, J = 5.6 Hz), 128.56, 128.13 (d, J = 5.6 Hz), 127.93 (d, J = 3.0 Hz), 127.91 (d, J = 17.3 Hz), 127.71 (dd, J = 4.3, 1.3 Hz), 127.37, 127.17 (d, J = 2.1 Hz), 125.97, 125.85 (d, J = 6.2 Hz), 125.73, 125.72, 125.69, 125.41, 121.74, 121.72, 121.62, 121.60, 117.50, 117.42 (dd, J = 9.6, 5.1 Hz), 117.35.
2-(quinolin-8-yl)-3,4-di-m-tolylisoquinolin-1(2H)-one (3ai). white solid (79%), mp 132.6-134.5°C. 1H NMR (400 MHz, CDCl3) δ 8.95 (ddd, J = 16.7, 4.2, 1.6 Hz, 1H), 8.64 – 8.47 (m, 1H), 8.07 (dd, J = 10.5, 3.9 Hz, 1H), 7.71 – 7.54 (m, 2H), 7.54 – 7.28 (m, 5H), 7.17 – 6.90 (m, 4H), 6.82 – 6.65 (m, 2H), 6.53 (t, J = 15.7 Hz, 2H), 6.37 (td, J = 7.6, 2.8 Hz, 1H), 2.33 – 2.14 (m, 3H), 1.81 (dd, J = 158.3, 5.8 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ = 162.7, 150.5, 141.8, 138.2, 137.9, 137.4, 137.1, 137.0, 136.5, 136.4, 136.1, 135.9, 135.9, 135.8, 135.7, 134.7, 132.6, 132.5, 132.4, 132.3, 131.6, 131.5, 130.9, 130.6, 130.5, 128.9, 128.8, 128.7, 128.5, 128.4, 128.3, 127.8, 127.8, 127.5, 127.5, 127.4, 127.4, 127.0, 126.9, 126.5, 126.40, 126.38, 126.2, 126.1, 125.9, 125.7, 125.5, 121.41, 121.39, 121.3, 118.5, 21.32, 21.25, 21.00, 20.56.

3-(4-chlorophenyl)-4-(4-fluorophenyl)-2-(quinolin-in-8-yl)isoquinolin-1(2H)-one (3aj) and 4-(4-chlorophenyl)-3-(4-fluorophenyl)-2-(quinolin-in-8-yl)isoquinolin-1(2H)-one (3ak). white solid (82%), 1H NMR (400 MHz, CDCl3) δ 8.90 (dd, J = 4.2, 1.7 Hz, 1H), 8.57 (dd, J = 7.9, 0.8 Hz, 1H), 8.12 – 8.02 (m, 1H), 7.71 (ddd, J = 8.2, 4.2, 1.3 Hz, 1H), 7.65 – 7.57 (m, 1H), 7.57 – 7.46 (m, 2H), 7.45 – 7.34 (m, 2H), 7.29 – 7.09 (m, 4H), 6.98 – 6.86 (m, 2H), 6.83 (dd, J = 8.2, 2.1 Hz, 1H), 6.77 – 6.67 (m, 1H), 6.59 – 6.46 (m, 1H), 6.22 (td, J = 8.6, 2.7 Hz, 1H). 13C NMR (101 MHz, CDCl3) δ = 161.69 (d, J = 246.5 Hz), 161.49 (d, J = 248.2 Hz), 162.7, 162.6, 150.8, 144.4, 141.0, 140.9, 137.9, 137.7, 137.34, 137.29, 136.2, 134.9, 133.4, 133.3, 133.13, 133.10, 133.05, 132.89, 132.87, 132.6, 132.36 (d, J = 8.3 Hz), 132.13 (d, J = 3.5 Hz), 131.9, 131.60 (d, J = 8.2 Hz), 131.1, 130.8, 130.70 (d, J = 3.5 Hz), 128.9, 128.8, 128.8, 128.49 (d, J = 8.4 Hz), 128.5, 128.3, 126.99 (d, J = 19.6 Hz), 127.0, 125.9, 125.76 (d, J = 20.9 Hz), 125.4, 125.3, 121.6, 117.7, 117.6, 115.4, 115.17 (d, J = 3.0 Hz), 115.0, 114.1, 113.89 (d, J = 1.5 Hz) 113.7. 19F NMR (376 MHz, CDCl3) δ = -113.02, -114.85.

3-(4-chlorophenyl)-2-(quinolin-8-yl)-4-(p-tolyliisoquinolin-1(2H)-one (3al) and 4-(4-chlorophenyl)-2-(quinolin-8-yl)-3-(p-tolyliisoquinolin-1(2H)-one (3am). white solid (90%). 1H NMR (400 MHz, CDCl3) δ = 8.97 – 8.87 (m, 1H), 8.56 (ddd, J = 8.0, 1.4, 1H), 8.06 (ddd, J = 7.2, 5.5, 1.6, 1H), 7.67 (ddd, J = 12.3, 8.2, 1.2, 1H), 7.59 (ddd, J = 8.4, 4.0, 2.0, 1H), 7.55 – 7.44 (m, 2H), 7.43 – 7.32 (m, 2H), 7.30 (d, J = 7.6, 1H), 7.22 (dd, J = 8.5, 2.1, 1H), 7.20 – 7.14 (m, 1H), 7.12 (dd, J = 11.4, 1.8, 1H), 7.10 – 6.97 (m, 3H), 6.91 (dd, J = 8.3, 2.0, 1H), 6.84 – 6.77 (m, 1H), 6.71 (dd, J = 8.1, 2.0, 1H), 6.65 (d, J = 7.7, 1H), 6.69 (dd, J = 7.9, 1.7, 1H), 6.47 (dd, J = 8.5, 2.1, 1H), 6.30 (d, J = 7.7, 1H), 2.82 (s, 2H), 1.95 (s, 1H). 13C NMR (101 MHz, CDCl3) δ = 162.7, 162.6, 150.8, 150.7, 144.6, 142.3, 140.5, 138.2, 137.9, 137.6, 137.5, 137.0, 136.5, 136.1, 136.0, 135.3, 133.6, 133.2, 133.1, 133.0, 132.97, 132.6, 132.5, 132.5, 132.0, 131.6, 131.5, 131.3, 131.2, 130.8, 130.76, 130.5, 129.4, 128.9, 128.81, 127.99, 127.89, 127.82, 128.49, 128.4, 128.3, 128.1, 127.6, 127.3, 126.9, 126.8, 126.7, 126.7, 125.8, 125.8, 125.6, 125.5, 125.2, 121.6, 121.5, 118.7, 117.2, 21.2, 21.0.
3,4-diethyl-2-(quinolin-8-yl)isoquinolin-1(2H)-one (3an), white solid (79%), mp 122.4-124.0°C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.86 (dd, $J = 4.2$, 1.7 Hz, 1H), 8.46 (dd, $J = 8.0$, 1.1 Hz, 1H), 8.24 (dd, $J = 8.3$, 1.7 Hz, 1H), 7.96 (dd, $J = 7.9$, 1.8 Hz, 1H), 7.78 (d, $J = 8.1$ Hz, 1H), 7.75 – 7.63 (m, 3H), 7.49 – 7.35 (m, 2H), 2.87 (q, $J = 7.5$ Hz, 2H), 2.57 (dd, $J = 14.9$, 7.5 Hz, 1H), 2.08 (dd, $J = 14.8$, 7.5 Hz, 1H), 1.33 (t, $J = 7.5$ Hz, 3H), 0.88 (t, $J = 7.5$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ = 163.2, 151.3, 144.8, 141.7, 137.44, 137.38, 136.3, 134.2, 132.4, 130.4, 129.3, 129.1, 128.7, 126.2, 125.62, 125.55, 123.9, 122.8, 121.8, 114.6, 23.6, 20.7, 14.9, 14.1.
4. References

5. Single-Crystal X-Ray Crystallography

5.1 Crystal structure of targeted isoquinolone 3ga'. The displacement ellipsoids are drawn at the 30% probability.
Table S1. Crystal data and structure refinement details for targeted 3ga'.

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\[a\text{ }R_1 = \Sigma |F_o| - |F_c| / \Sigma |F_o|. \text{ }b\text{ }wR_2 = \Sigma |w(F_o^2 - |F_c|^2)|/\Sigma |w(F_o)|^{1/2}|, \text{ where } w = 1 /[\sigma^2(F_o^2) + (aP)^2 + bP]. P = (F_o^2 + 2F_c^2)/3.\]
6. Copy of NMR (\textsuperscript{1}H, \textsuperscript{13}C, \textsuperscript{19}F) Spectra
Compound 1c
Compound 3aa
Compound 3ba
Compound 3ca
Compound 3da
Compound 3ea
Compound 3ea
Compound 3ga\textsuperscript{1}
Compound 3ga
Compound 3ha
Compound 3ia
Compound 3ab
S43
Compound 3ac
Compound 3ad
Compound 3ae

[Image of a chemical structure]
Compound 3af
Compound 3ag
Compound 3ai
Compound 3aj and 3ak
Compound 3al and 3am

1.7:1