Supporting Information

Magnesium iodide-catalyzed synthesis of 2-substituted quinazolines using

molecular oxygen and visible light

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1. General Information

Unless otherwise noted, all reactants or reagents including dry solvents were obtained from commercial suppliers and used as received. Flash column chromatography was performed with YMC-GEL SIL 8 nm S-25 um (SLF 08S25). Preparative thin-layer chromatography was carried out using 0.5 mm commercial silica gel plates (Merck silica gel 60 F_{254}). Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Merck silica gel 60 F_{254}). Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Merck silica gel 60 F_{254}). The developed chromatogram was analyzed by UV lamp (254 nm). ¹H NMR, ¹³C NMR and ¹⁹F NMR spectra were obtained on a JEOL ECA 500 spectrometer (500 MHz for ¹H NMR, 125 MHz for ¹³C NMR, and 470 MHz for ¹⁹F NMR). Chemical shifts (δ) are expressed in parts per million and are internally referenced [0.00 ppm (tetramethylsilane) for ¹H NMR and 77.0 ppm (CDCl₃) for ¹³C NMR]. High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-T100TD and are reported as m/z (relative intensity). Melting points were measured on a Yanaco micro melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer Spectrum 100 FTIR spectrometer and are reported in terms of frequency of absorption (cm⁻¹).

2. Preparation of Substrates

2-Aminobenzylamines (1c, 1d, 1e) and S-1b were prepared using modified literature procedures.¹

Preparation of 2-amino-6-methoxybenzamide (1b)



To a 50 mL of round-bottomed flask with a magnetic stirring bar were added LiAlH₄ (474.4 mg, 12.5 mmol) and THF (8 mL). The mixture was cooled to °C 0, then a solution of **S-1b** (421.5 mg, 2.5 mmol) in THF (8 mL) was added dropwise. The reaction mixture was stirred at reflux for 72 h. Then the mixture was cooled to room temperature, and 1 mL H₂O, 1 mL 15% aq. NaOH, and 3 mL H₂O were added at 0 °C subsequently. The suspension was filtered through celite and filter cake was washed with ethyl acetate (50 mL). The solution was extracted with ethyl acetate (20 mL x 3). The combined organic layers was dried over MgSO₄, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to furnish the desired product as a brown oil (51.7 mg, 14% yield).

¹H NMR (500 MHz, CDCl₃) δ 7.02 (t, *J* = 8.0 Hz, 1H), 6.35 (d, *J* = 8.0 Hz, 1H), 6.33 (d, *J* = 8.0 Hz, 1H), 3.92 (s, 2H), 3.79 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 157.9, 147.1, 128.1, 114.6, 109.2, 100.8, 55.4, 35.7. HRMS: m/z (DART) calcd for C₈H₁₃N₂O (M+H)⁺ 153.1028, found 153.1031. FTIR: (neat) 3358, 3222, 2939, 2837, 1623, 1587, 1471, 1440, 1382, 1330, 1266, 1202, 1174, 1155, 1088, 996, 909, 778, 730 cm⁻¹.

3. Synthesis of 2-syubtituted quinazolines

General

A solution of 2-aminobenzylamine (0.3 mmol), benzaldehyde (0.3 mmol) and magnesium iodide (5 mol%) in ethyl acetate (5 mL) in a pyrex test tube equipped with O_2 balloon was stirred and irradiated externally with a 23W fluorescent lamp placed at *ca*. 0.5 cm. The resulting mixture was directly concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to furnish the desired product.

2-Phenylquinazoline (3aa)² (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.29$ in *n*-hexane : ethyl acetate = 10 : 1). **3aa** was obtained as a yellow solid (54.0 mg, 87% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.48 (s, 1H), 8.62 (dd, J = 8.0, 1.7 Hz, 2H), 8.10 (dd, J = 8.6, 1.2 Hz, 1H), 7.95–7.90 (m, 2H), 7.63 (ddd, J = 8.0, 6.9, 1.2 Hz, 1H), 7.57–7.50

(m, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 161.1, 160.5, 150.8, 138.0, 134.1, 130.6, 128.6, 128.5, 127.3, 127.1, 123.6 (one carbon merged to others).

2-(4-Chlorophenyl)-quinazoline (3ab)² (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.4$ in *n*-hexane : ethyl acetate = 10 : 1). **3ab** was obtained as an ivory solid (60.2 mg, 83% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.45 (d, J = 1.2 Hz, 1H), 8.57 (d, J = 8.6 Hz, 2H), 8.07 (dd, J = 8.0, 1.2 Hz, 1H), 7.94–7.90 (m, 2H), 7.63 (ddd, J = 8.0, 6.9, 1.2 Hz,

1H), 7.50 (d, J = 8.6 Hz, 2H). ¹³C NMR (125 MHz, CDCl₃) δ 160.5, 160.0, 150.7, 136.8, 136.5, 134.3, 129.9, 128.8, 128.6, 127.4, 127.1, 123.6.

2-(4-Bromophenyl)-quinazoline (3ac)³ (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.42$ in *n*-hexane : ethyl acetate = 10 : 1). **3ac** was obtained as a white solid (68.5 mg, 80% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.46 (s, 1H), 8.51 (d, *J* = 8.6 Hz, 2H), 8.08 (d, *J* = 9.2 Hz, 1H), 7.95–7.91 (m, 2H), 7.68–7.63 (m, 3H). ¹³C NMR (125 MHz, CDCl₃)

 $\delta \ 160.6, \ 160.1, \ 150.7, \ 136.9, \ 134.3, \ 131.8, \ 130.1, \ 128.6, \ 127.5, \ 127.2, \ 125.4, \ 123.6.$

4-(2-Quinazolinyl)-benzoic acid methyl ester (3ad) (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.42$ in *n*-hexane : ethyl acetate = 10 : 1). **3ad** was obtained as an ivory solid (75.0 mg, 95% yield).

CO₂Me ¹H NMR (500 MHz, CDCl₃) δ 9.49 (s, 1H), 8.70 (d, J = 8.0 Hz, 2H), 8.20 (d, J = 8.0 Hz, 2H), 8.11 (d, J = 8.6 Hz, 1H), 7.96–7.92 (m, 2H), 7.66 (t, J = 8.0 Hz, 1H), 3.97 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 166.9, 160.6, 160.0, 150.6, 142.0, 134.3, 131.6, 129.8, 128.7, 128.4, 127.8, 127.1, 123.7, 52.2. m.p.: 162.2–162.9 °C. HRMS: m/z (DART) calcd for C₁₆H₁₃N₂O₂ (M+H)⁺ 265.0977, found 265.0975. FTIR: (neat) 3000, 2948, 1719, 1621, 1552, 1399, 1381, 1287, 1118, 863, 771, 712 cm⁻¹.

4-(2-Quinazolinyl)-benzonitrile (3ae)² (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.31$ in *n*-hexane : ethyl acetate = 10 : 1). **3ae** was obtained as a yellow solid (61.5 mg, 89% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.49 (s, 1H), 8.74 (d, J = 8.6 Hz, 2H), 8.11 (d, J = 8.0 Hz, 1H), 7.98–7.94 (m, 2H), 7.81 (d, J = 8.6 Hz, 2H), 7.69 (t, J = 8.0 Hz, 1H).

¹³C NMR (125 MHz, CDCl₃) δ 160.6, 159.0, 150.5, 142.1, 134.5, 132.3, 128.9, 128.7, 128.1, 127.2, 123.8, 118.9, 113.7.

2-(4-Nitrophenyl)-quinazoline (3af)⁴ (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.31$ in *n*-hexane : ethyl acetate = 10 : 1). **3af** was obtained as a yellow solid (71.2 mg, 94% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.52 (s, 1H), 8.82 (d, *J* = 8.6 Hz, 2H), 8.38 (d, *J* = NO₂ 8.6 Hz, 2H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.00–7.97 (m, 2H), 7.71 (dd, *J* = 8.0, 6.9

Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 160.7, 158.8, 150.6, 149.1, 143.8, 134.6, 129.4, 128.8, 128.3, 127.2, 123.9, 123.8.

2-(4-Methoxyphenyl)-quinazoline (3ag)² (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.35$ in *n*-hexane : ethyl acetate = 10 : 1). **3ag** was obtained as an ivory solid (14.5 mg, 21% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.43 (s, 1H), 8.58 (d, J = 9.2 Hz, 2H), 8.05 (d, J = 8.0 Hz, 1H), 7.91–7.87 (m, 2H), 7.58 (ddd, J = 8.0, 6.9, 1.2 Hz, 1H), 7.05 (d, J =

9.2 Hz, 2H), 3.90 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 161.8, 160.8, 160.4, 150.8, 134.0, 130.7, 130.2, 128.3, 127.1, 126.8, 123.3, 113.9, 55.4.

2-[4-(1,1-Dimethylethyl)phenyl]-quinazoline (3ah)² (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.43$ in *n*-hexane : ethyl acetate = 10 : 1). **3ah** was obtained as a yellow solid (73.2 mg, 93% yield). ¹H NMR (500 MHz, CDCl₃) δ 9.45 (s, 1H), 8.53 (d, J = 8.6 Hz, 2H), 8.08 (d, J =

t-Bu 8.6 Hz, 1H), 7.92–7.87 (m, 2H), 7.61–7.55 (m, 3H), 1.39 (s, 9H). ¹³C NMR (125

MHz, CDCl₃) δ 161.1, 160.4, 153.9, 150.8, 135.3, 134.0, 128.6, 128.3, 127.1, 127.0, 125.6, 123.5, 34.9, 31.3.

2-(4-Methylphenyl)-quinazoline (3ai)³ (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.59$ in *n*-hexane : ethyl acetate = 10 : 1). **3ai** was obtained as a yellow solid (59.1 mg, 89% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.43 (s, 1H), 8.51 (d, J = 8.0 Hz, 2H), 8.06 (d, J = 8.0 Hz, 1H), 7.90–7.86 (m, 2H), 7.57 (dd, J = 8.0, 7.5 Hz, 1H), 7.34 (d, J = 8.0 Hz, 36 NMR (125 MHz, CDCl) δ 161 1, 160 4, 150 8, 140 8, 125 3, 124 0, 120 4, 128 5

2H), 2.44 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 161.1, 160.4, 150.8, 140.8, 135.3, 134.0, 129.4, 128.5, 128.5, 127.1, 127.0, 123.5, 21.5.

2-(3-Methylphenyl)-quinazoline (3aj)³ (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.42$ in *n*-hexane : ethyl acetate = 10 : 1). **3aj** was obtained as a yellow solid (52.6 mg, 80% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.47 (s, 1H), 8.43–8.41 (m, 2H), 8.10 (d, *J* = 8.6 Hz, 1H), 7.94–7.90 (m, 2H), 7.62 (dd, *J* = 8.6, 6.9 Hz, 1H), 7.44 (dd, *J* = 8.0, 7.5 Hz,

1H), 7.34 (d, J = 7.5 Hz, 1H), 2.50 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 161.2, 160.5, 150.8, 138.3, 137.9, 134.1, 131.4, 129.1, 128.6, 127.2, 127.1, 125.8, 123.6, 21.5 (one carbon merged to others).

2-(3-Methoxyphenyl))-quinazoline (3ak)² (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.31$ in *n*-hexane : ethyl acetate = 10 : 1). **3ak** was obtained as a yellow solid (61.0 mg, 86% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.44 (s, 1H), 8.23–8.18 (m, 2H), 8.08 (d, J = 8.0 Hz, 1H), 7.91–7.87 (m, 2H), 7.59 (dd, J = 7.5, 6.9 Hz, 1H), 7.45 (dd, J = 8.0, 7.5 Hz, 1H), 7.07 (dd, J = 8.0, 2.3 Hz, 1H), 3.95 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 160.7, 160.4, 159.9,

150.6, 139.4, 134.0, 129.6, 128.6, 127.2, 127.0, 123.6, 121.1, 117.2, 112.9, 55.4.

2-(2-Methylphenyl)-quinazoline (3al)³ (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.43$ in *n*-hexane : ethyl acetate = 10 : 1). **3al** was obtained as a yellow liquid (56.0 mg, 85% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.50 (s, 1H), 8.10 (dd, J = 8.6, 1.2 Hz, 1H), 7.96–7.90 (m, 3H), 7.65 (ddd, J = 8.0, 6.9, 1.2 Hz, 1H), 7.39–7.33 (m, 3H), 2.61 (s, 3H). ¹³C

NMR (125 MHz, CDCl₃) δ 164.1, 160.2, 150.5, 138.7, 137.5, 134.3, 131.4, 130.7, 129.4, 128.7, 127.7, 127.2, 126.1, 123.0, 21.2.

2-(4-Pyridinyl)-quinazoline (3am)⁴ (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.34$ in *n*-hexane : ethyl acetate = 1 : 1). **3am** was obtained as a light brown solid (59.5 mg, 96% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.53 (d, J = 1.0 Hz, 1H), 8.83 (d, J = 5.8 Hz, 2H), 8.48 (d, J = 5.8 Hz, 2H), 8.15 (dd, J = 8.7, 1.0 Hz, 1H), 8.01–7.96 (m, 2H), 7.71 (ddd, J =

8.2, 6.8, 1.0 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 160.7, 158.9, 150.5, 145.2, 134.5, 128.8, 128.3, 127.2, 124.1, 122.3 (one carbon merged to others).

2-(2-Thienyl)-quinazoline (3an)² (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.29$ in *n*-hexane : ethyl acetate = 10 : 1). **3an** was obtained as an ivory solid (32.3 mg, 51% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.37 (s, 1H), 8.16 (dd, *J* = 3.9, 1.0 Hz, 1H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.91–7.88 (m, 2H), 7.59 (ddd, *J* = 8.2, 7.2, 1.0 Hz, 1H), 7.54 (dd, *J* = 4.8,

1.0 Hz, 1H), 7.21 (dd, *J* = 4.8, 3.9 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 160.5, 157.8, 150.6, 143.8, 134.3, 129.9, 129.2, 128.4, 128.1, 127.2, 127.0, 123.3.

5-Methoxy-2-phenylquinazoline (3ba) (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.21$ in *n*-hexane : ethyl acetate = 10 : 1). **3ba** was obtained as a white solid (43.1 mg, 61% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.80 (s, 1H), 8.62 (dd, *J* = 8.0, 1.7 Hz, 2H), 7.79 (t, *J* = 8.6 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.56–7.50 (m, 3H), 6.87 (d, *J* = 7.5 Hz, 1H), 4.04 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 161.4, 156.1, 156.1, 151.6, 138.1, 134.6, 130.5,

128.6, 128.6, 120.4, 115.9, 105.1, 55.8. m.p.: 150.7–151.3 °C. HRMS: m/z (DART) calcd for C₁₅H₁₃N₂O (M+H)⁺ 237.1028 found 237.1022. FTIR: (neat) 3060, 2959, 2834, 1619, 1575, 1558, 1470, 1433, 1391, 1376, 1345, 1281, 1252, 1215, 1173, 1115, 1070, 1047, 932, 902, 827, 792, 705, 693 cm⁻¹.

5-Fluoro-2-phenylquinazoline (3ca)⁵ (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.57$ in *n*-hexane : ethyl acetate = 10 : 1). **3ca** was obtained as a white solid (64.5 mg, 96% yield).

¹H NMR (500 MHz, CDCl₃) δ 9.71 (s, 1H), 8.62–8.60 (m, 2H), 7.87–7.78 (m, 2H), 7.55–7.50 (m, 3H), 7.20 (t, *J* = 8.6 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 161.6, 158.2 (d, *J* = 260.3 Hz), 154.8, 151.4, 137.5, 134.1 (d, *J* = 9.6 Hz), 130.9, 128.6 (d, *J* =

4.8 Hz), 124.5 (d, J = 3.6 Hz), 114.4 (d, J = 15.6 Hz), 110.9 (d, J = 18.0 Hz) (one carbon merged to others). ¹⁹F NMR (470 MHz, CDCl₃) δ -122.77 (dd, J = 9.0, 5.5 Hz).

6-Chloro-2-phenylquinazoline (3da)³ (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.57$ in *n*-hexane : ethyl acetate = 10 : 1). **3da** was obtained as a yellow solid (64.5 mg, 89% yield). ¹H NMR (500 MHz, CDCl₃) δ 9.37 (s, 1H), 8.59–8.57 (m, 2H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.87 (d, *J* = 2.3 Hz, 1H), 7.81 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.55–7.50 (m, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 161.2, 159.4, 149.2, 137.5, 135.0, 132.7, 130.8, 130.3, 128.7, 128.5, 125.8, 123.9.

7-Chloro-2-phenylquinazoline (3ea) (Table 2)



Purification by flash chromatography on silica gel ($R_f = 0.4$ in *n*-hexane : ethyl acetate = 10 : 1). **3ea** was obtained as a yellow solid (62.0 mg, 86% yield). ¹H NMR (500 MHz, CDCl₃) δ 9.45 (s, 1H), 8.62–8.60 (m, 2H), 8.10 (d, J = 1.7 Hz,

1H), 7.88 (d, J = 8.6 Hz, 1H), 7.58–7.53 (m, 4H). ¹³C NMR (125 MHz, CDCl₃) δ

161.8, 160.1, 151.2, 140.3, 137.5, 130.9, 128.6, 128.4, 128.3, 127.7, 121.8 (one carbon merged to others). m.p.: 137.1–137.7 °C. HRMS: m/z (DART) calcd for $C_{14}H_{10}CIN_2$ (M+H)⁺ 241.0532 found 241.0525. FTIR: (neat) 2925, 2853, 1611, 1584, 1566, 1542, 1451, 1399, 1278, 1237, 1187, 1021, 979, 935, 873, 797, 760, 700 cm⁻¹.

2-Phenyl-1,2,3,4-tetrahydroquinazoline (4aa)⁶ (Scheme 3)



A solution of 2-aminobenzylamine (5 mmol), and benzaldehyde (5 mmol) in ethyl acetate (30 mL) in a 100 mL flask equipped with N_2 balloon was stirred over night. The resulting mixture was directly concentrated in vacuo. The residue was recrystallized from CHCl₃. **4aa** was obtained as a white solid (779.5 mg, 74% yield).

¹H NMR (500 MHz, CDCl₃) δ 7.52 (dd, *J* = 8.6, 1.7 Hz, 2H), 7.41–7.33 (m, 3H), 7.05 (ddd, *J* = 8.0, 7.5, 1.2 Hz, 1H), 6.95 (dd, *J* = 7.5, 1.2 Hz, 1H), 6.72 (td, *J* = 7.5, 1.2 Hz, 1H), 6.59 (dd, *J* = 8.0, 1.2 Hz, 1H), 5.24 (s, 1H), 4.27 (d, *J* = 16.6 Hz, 1H), 4.20 (br, 1H), 4.00 (d, *J* = 16.6 Hz, 1H), 1.92 (br, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 143.7, 141.5, 128.7, 128.5, 127.3, 126.6, 126.2, 121.2, 118.1, 115.0, 69.6, 46.5.

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